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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 20 Jul 2006 (20060720/PD)
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8 "LOU SHENG C"/IN

thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2005058994 A1 20050317 APPLICATION: US 2004-940261 A1 20040914 (10)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 wherein said monoclonal antibody is 117-289.

# 2. (canceled)

3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 wherein said cell line is A.T.C.C. Deposit No. PTA-2806.

# 4-16. (canceled)

17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-I protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said at least one monoclonal antibody is 117-289; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.

### 18. (canceled)

- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151, 103-350, 115-303 and
- 20. A diagnostic reagent comprising at least one monoclonal antibody wherein said at least one monoclonal antibody is 117-289.

21-28. (canceled)

ANSWER 2 OF 8 USPATFULL on STN

2005:62890 Monoclonal antibodies to human immunodeficiency virus and uses thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2005053925 A1 20050310 APPLICATION: US 2004-940344 A1 20040914 (10) DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

What is claimed is:

- 1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 wherein said monoclonal antibody is 103-350.
- 2. (canceled)
- 3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said cell line is A.T.C.C. Deposit No. PTA-2808.

## 4-16. (canceled)

17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said at least one monoclonal antibody is 103-350; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.

- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151,  $\bar{1}17-289$ , 115B-303 and
- 20. A diagnostic reagent comprising at least one monoclonal antibody wherein said at least one monoclonal antibody is 103-350.

21-28. (canceled)

L1 ANSWER 3 OF 8 USPATFULL on STN

2005:62889 Monoclonal antibodies to human immunodeficiency virus and uses

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2005053924 A1 20050310 APPLICATION: US 2004-940262 A1 20040914 (10) DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1: A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said monoclonal antibody is 115B-303.

### 2. (canceled)

3: A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said cell line is A.T.C.C. Deposit No. PTA-2810.

### 4-16. (canceled)

17: A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 wherein said at least one monoclonal antibody is 115B-303; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.

## 18. (canceled)

- 19: The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 1 15B-151, 117-289, 103-350, and 108-394.
- 20: A diagnostic reagent comprising at least one monoclonal antibody wherein said at least one monoclonal antibody is 115B-303.

21-28. (canceled)

# ANSWER 4 OF 8 USPATFULL on STN

2005:62575 Monoclonal antibodies to human immunodeficiency virus and uses thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2005053610 A1 20050310 APPLICATION: US 2004-940392 Al 20040914 (10)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

What is claimed is:

1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said monoclonal antibody is 115B-151.

# 2. (canceled)

3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said cell line

4-16. (canceled)

-- ....... Doposie .... ... ....

- 17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 wherein said at least one monoclonal antibody is 115B-151; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.
- 18. (canceled)
- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 117-289, 103-350, 115B-303 and 108-394.
- 20. A diagnostic reagent comprising at least one monoclonal antibody wherein said at least one monoclonal antibody is 115B-151.
- 21-28. (canceled) .
- L1 ANSWER 5 OF 8 USPATFULL on STN
  2005:36949 Monoclonal antibodies to human immunodeficiency virus and uses

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2005031624 A1 20050210 APPLICATION: US 2004-940162 A1 20040914 (10) DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.
- 2. The monoclonal antibody of claim 1 wherein said antibody is 120A-270.
- 3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.
- 4. The hybridoma cell line of claim 3, wherein said line is A.T.C.C. Deposit No. HB PTA-3980.

5-16. (canceled)

- 17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.
- 18. The kit of claim 17 wherein said at least one monoclonal antibody of (a) is 120A-270.
- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 20. A diagnostic reagent comprising at least one monoclonal antibody wherein said at least one monoclonal antibody is 120A-270.
- 21-28. (canceled)
- L1 ANSWER 6 OF 8 USPATFULL on STN 2005:30342 Monoclonal antibodies to human immunodeficiency virus and uses thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES

US 2005025772 A1 20050203

APPLICATION: US 2004-940237 A1 20040914 (10)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said monoclonal antibody is 108-394.

### 2. (canceled)

3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said cell line is A.T.C.C. Deposit No. PTA-2807.

# 4-16. (canceled)

17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26, wherein said at least one monoclonal antibody is 108-394; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.

#### 18. (canceled)

- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350 and 115B-303.
- 20. A diagnostic reagent comprising at least one monoclonal antibody wherein said at least one monoclonal antibody is 108-394.

21-28. (canceled)

L1 ANSWER 7 OF 8 USPATFULL on STN 2004:133295 Monoclonal antibodies to human immunodeficiency virus and uses

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2004101831 A1 20040527

APPLICATION: US 2003-714689 A1 20031117 (10) DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.
- 2. The monoclonal antibody of claim 1 wherein said antibody is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus -2 protein p26.

4. The hybridoma cell line of claim 3, wherein said cell line	is
selected from the group consisting of A.T.C.C. Deposit No. HB	
A.T.C.C. Deposit No. HB , A.T.C.C. Deposit No. HB	. A.T.C.C.
Deposit No. HB, A.T.C.C. Deposit No. HB, and A.	r.c.c.
Deposit No. HB .	

5. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and b) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.

- 6. The method of claim 5 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 7. The method of claim 6 wherein said at least one monoclonal antibody of step (a) is labeled.
- 8. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation  $\ensuremath{\mathsf{P}}$ of antibody/antigen complexes; b) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.
- 9. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151 117-289, 103-350, 115B-303, and 108-394.
- 10. The method of claim 8 wherein said antibody of step (b) of said conjugate is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 11. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120-270, 108-394 and 115B-303, and said antibody of step (b) of said conjugate is selected from the group consisting of 117-289 and 115B-151.
- 12. The method of claim 11 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of step (b) of said conjugate is 115B-151.
- 13. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: (a) contacting: 1) at least one monoclonal antibody which binds to a shared epitope of HIV-1 p24 antigen and HIV-2 p26 antigen bound to a solid support, 2) said test sample, and 3) an indicator reagent comprising an antibody which binds to HIV-1 antigen and HIV-2 antigen to which a signal generating compound is attached, to form a mixture; (b) incubating said mixture for a time and under conditions sufficient to form antibody/antigen/antibody complexes; (c) detecting presence of a measurable signal generating by said signal-generating compound, presence of said signal indicating presence of one or more antigens in said test sample selected from the group consisting of HIV-1 antigen and HIV-2 antigen.
- 14. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 15. The method of claim 13 wherein said antibody of said indicator reagent of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 16. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of said indicator reagent of of step (a) is 115B-151.
- 17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.
- 18. The kit of claim 18 wherein said at least one monoclonal antibody of (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 19. The kit of claim 18 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-3-3

20. A diagnostic reagent comprising at least one monoclonal antibody selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 108-394 and 115B-303.

- 21. An isolated peptide comprising the amino acid sequence of SEQ ID  $\ensuremath{\mathsf{N0:1}}\xspace.$
- 22. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\sf NO:2.}$
- 23. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:3.}$
- $24.\ \mbox{An}$  isolated peptide comprising the amino acid sequence of SEQ ID NO:4.
- $25.\ \mbox{An isolated peptide comprising the amino acid sequence of SEQ ID NO:5.}$
- 26. An isolated peptide comprising the amino acid sequence of SEQ'ID NO:6.
- 27. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes; b) detecting said HIV-1 antigen/HIV-1 antibody complexes, presence of said complexes indicating presence of HIV-1 antibody in said test sample; c) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes; d) detecting said HIV-2 antigen/HIV-2 antibody complexes, presence of said, complexes indicating presence of HIV-2 antibody in said test sample; e) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and f) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.
- 28. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes: b) adding a conjugate to the resulting HIV-1 antigen/HIV-1 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; c) detecting HIV-1 antibody which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of HIV-1 antibody in said test sample; d) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes: 'e) adding a conjugate to the resulting HIV-2 antigen/HIV-2 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; f) detecting HIV-2 antibody which may be present in said test sample by detecting a signal generated by said signal-generating compound, presence of said signal indicating presence of HIV-2 antibody in said test sample; g) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; h) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and i) detecting presence of antigen which may be present in said test sample by detecting a signal

indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.

L1 ANSWER 8 OF 8 USPATFULL on STN

2002:198536 Monoclonal antibodies to human immunodeficiency virus and uses thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES
Hunt, Jeffrey C., Mundelein, IL, UNITED STATES
Konrath, John G., Lake Villa, IL, UNITED STATES
Qiu, Xiaoxing, Gurnee, IL, UNITED STATES
Scheffel, James W., Mundelein, IL, UNITED STATES
Tyner, Joan D., Beach Park, IL, UNITED STATES
US 2002106636 A1 20020808
APPLICATION: US 2000-731126 A1 20001206 (9)

DOCUMENT TYPE: Utility; APPLICATION. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.
- 2. The monoclonal antibody of claim 1 wherein said antibody is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 3. A hybridoma cell line which secretes a monoclonal antibody which binds to a shared epitope Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.
- 4. The hybridoma cell line of claim 3, wherein said cell line is selected from the group consisting of A.T.C.C. Deposit No. HB

  A.T.C.C. Deposit No. HB

  , A.T.C.C. Deposit No. HB

  , A.T.C.C. Deposit No. HB

  , and A.T.C.C. Deposit No. HB
- 5. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and b) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.
- 6. The method of claim 5 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 7. The method of claim 6 wherein said at least one monoclonal antibody of step (a) is labeled.
- 8. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human  ${\tt Immunodeficiency\ Virus-1\ protein\ 24\ and\ Human\ Immunodeficiency\ Virus-2}$ protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; b) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.
- 9. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151 117-289, 103-350, 115B-303, and 108-394.
- 10. The method of claim 8 wherein said antibody of step (b) of said conjugate is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 11. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120-270, 108-394

selected from the group consisting of 117-289 and 115B-151.

- 12. The method of claim 11 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of step (b) of said conjugate is 115B-151.
- 13. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: (a) contacting: 1) at least one monoclonal antibody which binds to a shared epitope of HIV-1 p24 antigen and HIV-2 p26 antigen bound to a solid support, 2) said test sample, and 3) an indicator reagent comprising an antibody which binds to HIV-1 antigen and HIV-2 antigen to which a signal generating compound is attached, to form a mixture; (b) incubating said mixture for a time and under conditions sufficient to form antibody/antigen/antibody complexes; (c) detecting presence of a measurable signal generating by said signal-generating compound, presence of said signal indicating presence of one or more antigens in said test sample selected from the group consisting of HIV-1 antigen and HIV-2 antigen.
- 14. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 15. The method of claim 13 wherein said antibody of said indicator reagent of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 16. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of said indicator reagent of of step (a) is 115B-151.
- 17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.
- 18. The kit of claim 17 wherein said at least one monoclonal antibody of (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-3-3 and 108-394.
- 20. A diagnostic reagent comprising at least one monoclonal antibody selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 108-394 and 115B-303.
- 21. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:1.}$
- 22. An isolated peptide comprising the amino acid sequence of SEQ ID  $\ensuremath{\mathsf{NO:2.}}$
- 23. An isolated peptide comprising the amino acid sequence of SEQ ID  $\ensuremath{\mathsf{NO:3.}}$
- $24\,.$  An isolated peptide comprising the amino acid sequence of SEQ ID NO:4.
- 25. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:5.}$
- 26. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:6.}$
- 27. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes; b) detecting said HIV-1 antigen/HIV-1 antibody complexes, presence of said complexes indicating presence of HIV-1 antibody in said test sample; c) contacting said test sample with at least one HIV-2 antigen

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28. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes: b) adding a conjugate to the resulting HIV-1 antigen/HIV-1 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; c) detecting HIV-1 antibody which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of HIV-1 antibody in said test sample; d) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes: e) adding a conjugate to the resulting HIV-2 antigen/ $\dot{\text{HIV-2}}$  antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; f) detecting HIV-2 antibody which may be present in said test sample by detecting a signal generated by said signal-generating compound, presence of said signal indicating presence of HIV-2 antibody in said test sample; g) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; h) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and i) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.

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ANSWER 1 OF 1 USPATFULL on STN 2002:198536 Monoclonal antibodies to human immunodeficiency virus and uses thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2002106636 A1 20020808 APPLICATION: US 2000-731126 A1 20001206 (9)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. What is claimed is:

> 1. A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.

- 2. The monoclonal antibody of claim 1 wherein said antibody is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 3. A hybridoma cell line which secretes a monoclonal antibody which

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- 5. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and b) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.
- 6. The method of claim 5 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 7. The method of claim 6 wherein said at least one monoclonal antibody of step (a) is labeled.
- 8. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; b) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.
- 9. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151 117-289, 103-350, 115B-303, and 108-394.
- 10. The method of claim 8 wherein said antibody of step (b) of said conjugate is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 11. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120-270, 108-394 and 115B-303, and said antibody of step (b) of said conjugate is selected from the group consisting of 117-289 and 115B-151.
- 12. The method of claim 11 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of step (b) of said conjugate is 115B-151.
- 13. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: (a) contacting: 1) at least one monoclonal antibody which binds to a shared epitope of HIV-1 p24 antigen and HIV-2 p26 antigen bound to a solid support, 2) said test sample, and 3) an indicator reagent comprising an antibody which binds to HIV-1 antigen and HIV-2 antigen to which a signal generating compound is attached, to form a mixture; (b) incubating said mixture for a time and under conditions sufficient to form antibody/antigen/antibody complexes; (c) detecting presence of a measurable signal generating by said signal-generating compound, presence of said signal indicating presence of one or more antigens in said test sample selected from the group consisting of HIV-1 antigen and HIV-2 antigen.
- 14. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 15. The method of claim 13 wherein said antibody of said indicator reagent of step (a) is selected from the group consisting of 120A-270,

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16. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of said indicator reagent of of step (a) is 115B-151.

- 17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.
- 18. The kit of claim 17 wherein said at least one monoclonal antibody of (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-3-3 and 108-394.
- 20. A diagnostic reagent comprising at least one monoclonal antibody selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 108-394 and 115B-303.
- 21. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:1.}$
- 22. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:2.}$
- 23. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:3.}$
- 24. An isolated peptide comprising the amino acid sequence of SEQ ID NO:4.
- 25. An isolated peptide comprising the amino acid sequence of SEQ ID  $\ensuremath{\mathsf{NO:5}}\xspace.$
- 26. An isolated peptide comprising the amino acid sequence of SEQ ID NO:6.
- 27. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes; b) detecting said HIV-1 antigen/HIV-1 antibody complexes, presence of said complexes indicating presence of HIV-1 antibody in said test sample; c) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes; d) detecting said HIV-2 antigen/HIV-2 antibody complexes, presence of said complexes indicating presence of HIV-2 antibody in said test sample; e) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and f) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.
- 28. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes: b) adding a conjugate to the resulting HIV-1 antigen/HIV-1 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; c) detecting HIV-1 antibody which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of HIV-1 antibody in said test sample; d) contacting said test sample

mich de roube one mi, e amergen maron brido eo mi, e amerboaj roi d and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes: e) adding a conjugate to the resulting HIV-2 antigen/HIV-2 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; f) detecting HIV-2 antibody which may be present in said test sample by detecting a signal generated by said signal-generating compound, presence of said signal indicating presence of HIV-2 antibody in said test sample; g) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; h) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and i) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.

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E1
                   HUNT JEFFREY A/IN
E2
                   HUNT JEFFREY B/IN
E3
            18 --> HUNT JEFFREY C/IN
E4
            1
                   HUNT JEFFREY D/IN
                   HUNT JEFFREY E/IN
E.5
            2
E6
                   HUNT JEFFREY GLENN/IN
             1
                   HUNT JEFFREY H/IN
E7
            40
                   HUNT JEFFREY M/IN
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                   HUNT JEFFREY SCOTT/IN
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ΤI
       Antigen cocktails, P35, and uses thereof
L5
    ANSWER 2 OF 10 USPATFULL on STN
       Mouse monoclonal antibody (5-21-3) to human immunodeficiency virus
TI
       gp41 protein
     ANSWER 3 OF 10 USPATFULL on STN
L_5
ΤI
       Antigen cocktails and uses thereof
    ANSWER 4 OF 10 USPATFULL on STN
L5
ΤI
       Antigen cocktails and uses thereof
    ANSWER 5 OF 10 USPATFULL on STN
1.5
TI
       Method of using P35 antigen of toxoplasma gondii in distinguishing acute
       from chronic toxoplasmosis
    ANSWER 6 OF 10 USPATFULL on STN
L5
       Borrelia burgdorferi antigens and uses thereof
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- ΤI Borrelia burgdorferi antigens and uses thereof
- ANSWER 9 OF 10 USPATFULL on STN 1.5
- Monoclonal antibody for differentiating HIV-2 from HIM-1 seropositive ΤI individuals
- L5 ANSWER 10 OF 10 USPATFULL on STN
- Mouse monoclonal antibodies to hiv-1p24 and their use in diagnostic TΤ
- => d 15,cbib,clm,1-4,9,10
- ANSWER 1 OF 10 USPATFULL on STN 2003:173209 Antigen cocktails, P35, and uses thereof. Maine, Gregory T., Gurnee, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Brojanac, Susan, Brookfield, WI, UNITED STATES Sheu, Michael Jyh-Tsing, Gurnee, IL, UNITED STATES Chovan, Linda E., Kenosha, WI, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES Howard, Lawrence V., Libertyville, IL, UNITED STATES Parmley, Stephen F., San Jose, CA, UNITED STATES Remington, Jack S., Menlo Park, CA, UNITED STATES Araujo, Fausto, Palo Alto, CA, UNITED STATES Suzuki, Yashuhiro, Menlo Park, CA, UNITED STATES Li, Shuli, San Jose, CA, UNITED STATES US 2003119053 A1 20030626 APPLICATION: US 2000-728644 A1 20001201 (9) DOCUMENT TYPE: Utility; APPLICATION. CAS INDEXING IS AVAILABLE FOR THIS PATENT.
- What is claimed is:
  - 1. A composition comprising Toxoplasma gondii antigens P29, P30 and P35.
  - 2. A composition comprising Toxoplasma gondii antigens P29, P35 and P66.
  - 3. The composition of claim 1 or 2 wherein said composition is a diagnostic reagent.
  - 4. The composition of claim 1 or 2 wherein said antigens are produced by recombinant or synthetic means.
  - 5. An isolated nucleic acid sequence represented by SEQ ID NO: 26.
  - 6. A purified polypeptide having the amino acid sequence represented by SEQ ID NO: 27.
  - 7. A polyclonal or monoclonal antibody directed against said purified polypeptide of claim 6.
  - 8. A method for detecting the presence of  $\operatorname{IgM}$  antibodies to  $\operatorname{Toxoplasma}$ gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM antibodies with a composition comprising P29, P35 and P66; and b) detecting the presence of said IgMantibodies.
  - 9. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM antibodies with a composition comprising antigen P29, P35 and P66 for a time and under conditions sufficient for the formation of IgM antibody/antigen complexes; b) adding a conjugate to the resulting IgM antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting the presence of IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
  - 10. The method according to claim 9 wherein said composition further comprises P30.
  - 11. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG antibodies with a composition comprising P29, P30 and P35; and b) detecting the presence of said IgG antibodies.
  - 12. A method for detecting the presence of IgG antibodies to

contacting said test sample suspected of containing said IgG antibodies with a composition comprising antigen P29, P30 and P35 for a time and under conditions sufficient for formation of IgG antibody/antigen complexes; b) adding a conjugate to resulting IgG antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.

- 13. The method according to claim 12 wherein said composition further comprises P66.
- 14. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM antibodies with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM antibody complexes; b) adding a conjugate to resulting anti-antibody/IgM antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a composition comprising P29, P35 and P66, each attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 15. The method according to claim 14 wherein said composition further comprises  ${\tt P30}.$
- 16. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG antibodies with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgG antibody complexes; b) adding a conjugate to resulting anti-antibody/IgG antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a composition comprising P29, P30 and P35, each attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 17. The method according to claim 16 wherein said composition further comprises P66.
- 18. A vaccine comprising: 1) Toxoplasma gondii antigens P29, P30 and P35 and 2) a pharmaceutically acceptable adjuvant.
- 19. A vaccine comprising: 1) Toxoplasma gondii antigens P29, P35 and P66 and 2) a pharmaceutically acceptable adjuvant.
- 20. A kit for determining the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising: a) a composition comprising Toxoplasma gondii antigens P29, P35 and P66; and b) a conjugate comprising an **antibody** attached to a signal generating compound capable of generating a detectable signal.
- 21. A kit for determining the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising: a) a composition comprising Toxoplasma gondii antigens P29, P30 and P35; and b) a conjugate comprising an **antibody** attached to a signal generating compound capable of generating a detectable signal.
- 22. A kit for determining the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgM **antibody**; and b) a composition comprising Toxoplasma gondii antigens P29, P35 and P66.
- 23. A kit for determining the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgM **antibody**; b) a conjugate comprising: 1) Toxoplasma gondii antigens P29, P35 and P66, each attached to 2) a signal generating compound capable of generating a detectable signal.
- 24. A kit for determining the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgG **antibody**; and b) a composition comprising Toxoplasma gondii antigens P29, P35 and P66.

gondii in a test sample comprising: a) an anti-antibody specific for IgG antibody: b) a conjugate comprising: 1) Toxoplasma gondii antigens P29, P35 and P66, each attached to 2) a signal generating compound capable of generating a detectable signal.

- 26. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgM antibodies with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody IgM complexes; (b) adding antigen to resulting anti-antibody/IgM complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgM antibody, said antigen comprising a mixture of P29, P35 and P66; and (c) adding a conjugate to resulting anti-antibody/IgM/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal antibody attached to a signal generating compound capable of generating a detectable signal; and (d) detecting IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- $27.\ \mbox{The method}$  according to claim  $26\ \mbox{wherein}$  said mixture further comprises P30.
- 28. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgG antibodies with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody IgG complexes; (b) adding antigen to resulting anti-antibody/IgG complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgG antibody, said antigen comprising a mixture of P29, P30 and P35; and (c) adding a conjugate to resulting anti-antibody/IgG/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal antibody attached to a signal generating compound capable of generating a detectable signal; and (d) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 29. The method according to claim 28 wherein said mixture further comprises P66.
- 30. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM and IgM antibodies with a composition comprising antigen P29, P30, P35 and P66 for a time and under conditions sufficient for the formation of IgM antibody/antigen complexes; b) adding a conjugate to the resulting IgM antibody/antigen complexes and IgG antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound IgM and IgG antibody, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting the presence of IgM and IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 31. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM and IgG antibodies with anti-antibody specific for said IgM antibodies and said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM antibody complexes and anti-antibody/IgG antibody complexes; b) adding a conjugate to resulting anti-antibody/IgM antibody complexes and resulting anti-antibody/IgM antibody complexes and resulting anti-antibody/IgG antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises P29, P30, P35 and P66, each attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 32. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgM and IgG antibodies with anti-antibody specific for said IgM antibodies and with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM complexes and anti-antibody/IgG complexes; (b) adding antigen to resulting anti-antibody/IgM complexes amd resulting anti-antibody/IgG complexes for a time and under conditions sufficient

comprising a mixture of P29, P30, P35 and P66; and (c) adding a conjugate to resulting anti-antibody/IgM/antigen complexes and anti-antibody/IgG/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal antibody attached to a signal generating compound capable of generating a detectable signal; and (d) detecting IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.

- 33. A method of producing monoclonal **antibodies** comprising the steps of: a) injecting a non-human mammal with an antigen; b) administering a composition comprising antibiotics to said non-human mammal; c) injecting said non-human mammal with said antigen; d) fusing spleen cells of said non-human mammal with myeloma cells in order to generate hybridomas; and e) culturing said hybridomas under sufficient time and conditions such that said hybridomas produce monoclonal **antibodies**.
- 34. The method of claim 34 wherein said antigen is derived from an organism selected from the group consisting of Borrelia burgdorferi, Schistosoma treponema, Toxoplasma gondii, Plasmodium vivax and Plasmodium falciparum.
- $35.\ A$  composition comprising the isolated nucleic acid sequence represented by FIG. 11 or a fragment thereof.
- 36. A composition comprising amino acids 1-135 of P35.
- $37.\ \mbox{The composition of claim }35\ \mbox{or }36\ \mbox{wherein said composition is a diagnostic reagent.}$
- 38. A method for distinguishing between acute and chronic Toxoplasmosis in a patient suspected of having either said acute or chronic Toxoplasmosis comprising the steps of: a) contacting a test sample, from said patient, with a composition comprising amino acids 1-135 of P35; and b) detecting the presence of IgG antibodies, presence of said IgG antibodies indicating acute Toxoplasmosis in said patient and lack of said IgG antibodies indicating chronic Toxoplasmosis in said patient.
- 39. A kit for distinguishing between acute and chronic Toxoplasmosis in a patient suspected of having either said acute Toxoplasmosis or said chronic Toxoplasmosis comprising: a) a composition comprising amino acids 1-135 of Toxoplasma gondii antigen P35; and b) a conjugate comprising an **antibody** attached to a signal generating compound capable of generating a detectable signal.
- 40. A kit for distinguishing between acute and chronic Toxoplasmosis in a patient suspected of having either said acute Toxoplasmosis or said chronic Toxoplasmosis comprising: a) an anti-antibody specific for IgG antibody; and b) a conjugate comprising amino acids 1-135 of Toxoplasma gondii antigen P35 attached to a signal generating compound capable of generating a detectable signal.
- L5 ANSWER 2 OF 10 USPATFULL on STN 2003:173141 Mouse monoclonal **antibody** (5-21-3) to human immunodeficiency virus gp41 protein.

Hunt, Jeffrey C., Lindenhurst, IL, UNITED STATES Dawson, George J., Libertyville, IL, UNITED STATES Sarin, Virender K., Libertyville, IL, UNITED STATES Webber, J. Scott, Waukegan, IL, UNITED STATES Wray, Larry K., Highland Park, IL, UNITED STATES Falk, Lawrence A., Waukegan, IL, UNITED STATES Devare, Sushil G., Northbrook, IL, UNITED STATES US 2003118985 Al 20030626
APPLICATION: US 2001-86409 Al 20011119 (10) DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A monoclonal **antibody** characterized by its specificity for an epitope on HIV I gp41 formed by a first sequence of amino acids Ile-His-Ser-Leu-Ile-Glu-Ser-Gln-Asn-Gln-Glu-Lys-Asn-Glu-Gln-Glu-L eu-Leu-Glu-Leu-Asp-Lys with at least one flanking amino acid sequence of at least 5 amino acids in length either 3' to the carboxy terminus or 5' to the amino terminus of said first sequence, said flanking sequence having an amino acid sequence substantially corresponding to that found on native HIV I gp41 adjacent said first sequence, said flanking sequence putting said first sequence into proper antigenic conformation.

- 2. An immortal, mammalian **antibody**-producing cell line that produces the monoclonal **antibody** of claim 1.
- 3. The cell line of claim 2, wherein said cell line is a hybridoma which

fused to myeloma cell line SP2/0.

- 4. A murine derived hybridoma cell line ATCC HB 9628.
- 5. A monoclonal antibody produced by the hybridoma cell line ATCC 9628 designated the 5-21-3 monoclonal antibody.
- 6. A method for detecting a marker indicative of exposure to HIV I in a sample comprising forming an <code>antibody/antigen</code> complex between the epitope on HIV I gp41 formed by a first sequence of amino acids Ile-His-Ser-Leu-Ile-Glu-Glu-Ser-Gln-Asn-Gln-Glu-Lys-Asn-Glu-Glu-Glu-Leu-Glu-Leu-Asp-Lys with at least one flanking amino acid sequence of at least 5 amino acids in length either 3' to the carboxy terminus or 5' to the amino terminus of said first sequence, said flanking sequence having an amino acid sequence substantially corresponding to that found on native HIV I gp41 adjacent said first sequence and a <code>antibody</code> specific for that epitope, and detecting the presence or amount of the <code>antibody/antigen</code> complex formed.
- 7. The method of claim 6 wherein the **antibody**/antigen complex is formed in an immunometric, competitive, sandwich, or agglutination assay format.
- 8. The method of claim 6 wherein the antibody is a monoclonal antibody.
- 9. The method of claim 8 wherein the monoclonal **antibody** is the monoclonal **antibody** of claims 1 or 5.
- 10. The method of claim 9 wherein the monoclonal  $\mbox{antibody}$  is labeled with a detectable label.
- 11. The method of claim 10 wherein said label comprises a radioisotope, enzyme, fluorescent compound, chemiluminescent compound or member of a specific binding pair.
- 12. An immunoassay for determining the presence or amount of antibody to HIV I gp41 in a test sample comprising incubating the test sample with a solid phase-bound binding material containing a target epitope having the immunological properties of the epitope on HIV I gp41 formed by a first sequence of amino acids Ile-His-Ser-Leu-Ile-Glu-Glu-Ser-Gln-Asn-Gln-Glu-Lys-Asn-Glu-Glu-Glu-Leu-Asp-Lys with at least one flanking amino acid sequence of at least 5 amino acids in length either 3' to the carboxy terminus or 5' to the amino terminus of said first sequence, said flanking sequence having an amino acid sequence substantially corresponding to that found on native HIV I gp41 adjacent said first sequence and with a probe antibody which specifically binds to the target epitope of the binding material, and then determining the presence or amount of the probe antibody bound or unbound to the binding material as an indication of the presence or amount of antibody to HIV I gp41 in the test sample.
- 13. The immunoassay of claim 12, wherein said binding material comprises partially purified HIV I, native HIV I gp41, or full-length recombinant-derived gp41.
- 14. The immunoassay of claim 13, wherein said binding material is the recombinant product of the cloned BglII to KpnI restriction fragment of HIV I gp41 bound to said solid phase via human IgG positive for said gp41.
- 15. The immunoassay of claim 14, wherein the probe **antibody** is a monoclonal **antibody** of claims 1 or 5.
- 16. The immunoassay of claim 12 wherein the probe antibody is a monoclonal antibody.
- 17. The immunoassay of claim 16 wherein the monoclonal  ${\bf antibody}$  is the monoclonal  ${\bf antibody}$  of claims 1 or 5.
- 18. The immunoassay of claim 17 wherein the monoclonal **antibody** is labelled with a detectable label.
- 19. The immunoassay of claim 12, wherein the presence or amount of the probe **antibody** bound or unbound to the binding material is determined by incubating said probe **antibody** with a labeled anti-species, second **antibody**.
- 20. The immunoassay of claims 18 or 19 wherein said label comprises a radioisotope, enzyme, fluorescent compound, chemiluminescent compound, or member of a specific binding pair.
- 21. A diagnostic kit for detection of exposure to HIV I comprising the

L5 ANSWER 3 OF 10 USPATFULL on STN
2002:43176 Antigen cocktails and uses thereof.
Maine, Gregory T., Gurnee, IL, UNITED STATES

Brunt, Jeffrey C., Mundelein, IL, UNITED STATES
Brojanac, Susan, Brookfield, WI, UNITED STATES
Sheu, Michael Jyh-Tsing, Gurnee, IL, UNITED STATES
Chovan, Linda E., Kenosha, WI, UNITED STATES
Tyner, Joan D., Beach Park, IL, UNITED STATES
Howard, Lawrence V., Libertyville, IL, UNITED STATES
US 2002025542 Al 20020228
APPLICATION: US 2001-896852 Al 20010629 (9)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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CLM What is claimed is:

- 1. A composition comprising Toxoplasma gondii antigens P29, P30 and P35.
- 2. A composition comprising Toxoplasma gondii antigens P29, P35 and P66.
- 3. The composition of claims  $1\ \mathrm{or}\ 2$  wherein said composition is a diagnostic reagent.
- 4. The composition of claims  $1\ \mathrm{or}\ 2$  wherein said antigens are produced by recombinant or synthetic means.
- 5. An isolated nucleic acid sequence represented by SEQ ID NO: 26.
- 6. A purified polypeptide having the amino acid sequence represented by SEQ ID No: 27.
- 7. A polyclonal or monoclonal  $\mbox{antibody}$  directed against said purified polypeptide of claim 6.
- 8. A method for detecting the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM **antibodies** with a composition comprising P29, P35 and P66; and b) detecting the presence of said IgM **antibodies**.
- 9. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM antibodies with a composition comprising antigen P29, P35 and P66 for a time and under conditions sufficient for the formation of IgM antibody/antigen complexes; b) adding a conjugate to the resulting IgM antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting the presence of IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 11. A method for detecting the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG **antibodies** with a composition comprising P29, P30 and P35; and b) detecting the presence of said IgG **antibodies**.
- 12. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG antibodies with a composition comprising antigen P29, P30 and P35 for a time and under conditions sufficient for formation of IgG antibody/antigen complexes; b) adding a conjugate to resulting IgG antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 13. The method according to claim 12 wherein said composition further comprises P66.
- 14. A method for detecting the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM **antibodies** with anti-**antibody** specific for said IgM **antibodies** for

anti-antibody/IgM antibody complexes; b) adding a conjugate to resulting anti-antibody/IgM antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a composition comprising P29, P35 and P66, each attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.

- 15. The method according to claim 14 wherein said composition further comprises  ${\sf P30}$ .
- 16. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG antibodies with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgG antibody complexes; b) adding a conjugate to resulting anti-antibody/IgG antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a composition comprising P29, P30 and P35, each attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- $17.\ \mbox{The method}$  according to claim 16 wherein said composition further comprises P66.
- 18. A vaccine comprising: 1) Toxoplasma gondii antigens P29, P30 and P35 and 2) a pharmaceutically acceptable adjuvant.
- 19. A vaccine comprising: 1) Toxoplasma gondii antigens P29, P35 and P66 and 2) a pharmaceutically acceptable adjuvant.
- 20. A kit for determining the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising: a) a composition comprising Toxoplasma gondii antigens P29, P35 and P66; and b) a conjugate comprising an **antibody** attached to a signal generating compound capable of generating a detectable signal.
- 21. A kit for determining the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising: a) a composition comprising Toxoplasma gondii antigens P29, P30 and P35; and b) a conjugate comprising an **antibody** attached to a signal generating compound capable of generating a detectable signal.
- 22. A kit for determining the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgM **antibody**; and b) a composition comprising Toxoplasma gondii antigens P29, P35 and P66.
- 23. A kit for determining the presence of IgM **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgM **antibody**; b) a conjugate comprising: 1) Toxoplasma gondii antigens P29, P35 and P66, each attached to 2) a signal generating compound capable of generating a detectable signal.
- 24. A kit for determining the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgG **antibody**; and b) a composition comprising Toxoplasma gondii antigens P29, P35 and P66.
- 25. A kit for determining the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising: a) an anti-**antibody** specific for IgG **antibody**; b) a conjugate comprising: 1) Toxoplasma gondii antigens P29, P35 and P66, each attached to 2) a signal generating compound capable of generating a detectable signal.
- 26. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgM antibodies with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody IgM complexes; (b) adding antigen to resulting anti-antibody/IgM complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgM antibody, said antigen comprising a mixture of P29, P35 and P66; and (c) adding a conjugate to resulting anti-antibody/IgM/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal antibody attached to a signal generating compound capable of generating a detectable signal; and (d) detecting IgM antibodies which may be present in said test

compound.

- 27. The method according to claim 26 wherein said mixture further comprises P30.
- 28. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgG antibodies with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody IgG complexes; (b) adding antigen to resulting anti-antibody/IgG complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgG antibody, said antigen comprising a mixture of P29, P30 and P35; and (c) adding a conjugate to resulting anti-antibody/IgG/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal antibody attached to a signal generating compound capable of generating a detectable signal; and (d) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 29. The method according to claim 28 wherein said mixture further comprises P66.
- 30. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM and IgM antibodies with a composition comprising antigen P29, P30, P35 and P66 for a time and under conditions sufficient for the formation of IgM antibody/antigen complexes; b) adding a conjugate to the resulting IgM antibody/antigen complexes and IgG antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound IgM and IgG antibody, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting the presence of IgM and IgM antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 31. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM and IgG antibodies with anti-antibody specific for said IgM antibodies and said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM antibody complexes and anti-antibody/IgG antibody complexes; b) adding a conjugate to resulting anti-antibody/IgM antibody complexes and resulting anti-antibody/IgM antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises P29, P30, P35 and P66, each attached to a signal generating compound capable of generating a detectable signal; and c) detecting IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 32. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing  $\operatorname{IgM}$  and  $\operatorname{IgG}$ antibodies with anti-antibody specific for said IgM antibodies and with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM complexes and anti-antibody/IgG complexes; (b) adding antigen to resulting anti-antibody/IgM complexes amd resulting anti-antibody/IgG complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgM antibody, said antigen comprising a mixture of P29, P30, P35 and P66; and (c) adding a conjugate to resulting anti-antibody/IgM/antigen complexes and anti-antibody/IgG/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal antibody attached to a signal generating compound capable of generating a detectable signal; and (d) detecting IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal generating compound.
- 33. A method of producing monoclonal **antibodies** comprising the steps of: e) injecting a non-human mammal with an antigen; f) administering a composition comprising antibiotics to said non-human mammal; g) injecting said non-human mammal with said antigen; h) fusing spleen cells of said non-human mammal with myeloma cells in order to generate hybridomas; and i) culturing said hybridomas under sufficient time and conditions such that said hybridomas produce monoclonal **antibodies**.
- 34. The method of claim 34 wherein said antigen is derived from an

Schistosoma treponema, Toxoplasma gondii, Plasmodium vivax and Plasmodium falciparum.

L5 ANSWER 4 OF 10 USPATFULL on STN

2001:226423 Antigen cocktails and uses thereof.

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US 6329157 B1 20011211

APPLICATION: US 1998-86503 19980528 (9)

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. A method for detecting the presence of IgM antibodies to Toxoplasma gondii (T. gondii) in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM antibodies with a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55; and b) detecting the presence of said IgM antibodies.
- 2. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IqM antibodies with a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55, for a time and under conditions sufficient for the formation of IqM antibody/antigen complexes; b) adding a conjugate to the resulting IgM antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an anti-IgM antibody attached to a signal-generating compound capable of generating a detectable signal; and c) detecting the presence of IgM antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compound.
- 3. The method according to claim 2 wherein said composition further comprises a fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53.
- 4. A method for detecting the presence of IgG **antibodies** to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG **antibodies** with a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53, and a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54; and b) detecting the presence of said IgG **antibodies**.
- 5. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG antibodies with a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53, and a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, for a time and under conditions sufficient for formation of IgG antibody/antigen complexes; b) adding a conjugate to resulting IgG antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises an anti-IgG antibody attached to a signal-generating compound capable of generating a detectable signal; and c) detecting IgG antibodies which may be present in said test

compound.

- 6. The method according to claim 5 wherein said composition further comprises a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55.
- 7. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM antibodies with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM antibody complexes; b) adding a conjugate to resulting anti-antibody/IgM antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55, each attached to a signal-generating compound capable of generating a detectable signal; and c) detecting IgM antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compound.
- 8. The method according to claim 7 wherein said composition further comprises a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53.
- 9. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgG antibodies with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgG antibody complexes; b) adding a conjugate to resulting anti-antibody/IgG antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEO ID NO:53, and a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, each attached to a signal-generating compound capable of generating a detectable signal; and c) detecting IgG antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compounds.
- 10. The method according to claim 9 wherein said composition further comprises a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55.
- 11. A method for detecting the presence of IgM antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgM antibodies with anti-antibody specific for said IgM antibodies for a time and under conditions sufficient to allow for formation of anti-antibody IgM complexes; (b) adding an antigen to resulting anti-antibody/IgM complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgM antibody, said antigen comprising a mixture of a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55; and (c) adding a conjugate to resulting anti-antibody/IgM/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal anti-IgM antibody attached to a signal-generating compound capable of generating a detectable signal; and (d) detecting IgM antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compound.
- 12. The method according to claim 11 wherein said mixture further comprises a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53.

- 13. A method for detecting the presence of IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgG antibodies with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody IgG complexes; (b) adding an antigen to resulting anti-antibody/IgG complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgG antibody, said antigen comprising a mixture a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53, and a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54; (c) adding a conjugate to resulting anti-antibody/IgG/antigen complexes, said conjugate comprising a composition comprising monoclonal or polyclonal IgG antibody attached to a signal-generating compound capable of generating a detectable signal; and (d) detecting IgG antibodies which may be present in said test sample by-detecting a signal generated by said signal-generating compound.
- 14. The method according to claim 13 wherein said mixture further comprises a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55.
- 15. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM and IgG antibodies with a composition comprising a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55, for a time and under conditions sufficient for the formation of IgM antibody/antigen complexes and IgG antibody/antigen complexes; b) adding a first conjugate to resulting IgM antibody/antigen complexes and a second conjugate to resulting IgG antibody/antigen complexes for a time and under conditions sufficient to allow said first and second conjugates to bind to the bound IgM and IgG antibody, respectively, wherein said first conjugate comprises an anti-IgM antibody attached to a signal- generating compound capable of generating a detectable signal and said second conjugate comprises an anti-IgG  ${\tt antibody}$ attached to a signal-generating compound capable of generating a detectable signal; and c) detecting the presence of IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compounds.
- 16. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: a) contacting said test sample suspected of containing said IgM and IgG antibodies with anti-antibody specific for said IgM antibodies and said IgG antibodies for a time and under conditions sufficient to allow for formation of anti-antibody/IgM antibody complexes and anti-antibody/IgG antibody complexes; b) adding a conjugate to resulting anti-antibody/IgM antibody complexes and resulting anti-antibody/IgG antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to bound antibody, wherein said conjugate comprises a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55, each attached to a signal-generating compound capable of generating a detectable signal; and c) detecting IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compounds.
- 17. A method for detecting the presence of IgM and IgG antibodies to Toxoplasma gondii in a test sample comprising the steps of: (a) contacting said test sample suspected of containing IgM and IgG antibodies with anti-antibody specific for said IgM antibodies and with anti-antibody specific for said IgG antibodies for a time and under conditions sufficient to allow for formation of

and with the state of the completened and and with the same of the completened, adding an antigen to resulting anti-antibody/IgM complexes and resulting anti-antibody/IgG complexes for a time and under conditions sufficient to allow said antigen to bind to bound IgM and IgG antibody, respectively, said antigen comprising a mixture of a recombinant P29 antigen of T. gondii comprising SEQ ID NO:27, a recombinant fusion protein comprising a portion of the P30 antigen of T. gondii, said portion of said P30 antigen corresponding to amino acids 175-459 of SEQ ID NO:53, a recombinant fusion protein comprising a portion of the P35 antigen of T. gondii, said portion of said P35 antigen corresponding to amino acids 172-306 of SEQ ID NO:54, and a recombinant fusion protein comprising a portion of the P66 antigen of T. gondii, said portion of said P66 antigen corresponding to amino acids 173-575 of SEQ ID NO:55; and (c) adding a first conjugate to resulting anti-antibody/IgM/antigen complexes and a second conjugate to resulting anti-antibody/IgG/antigen complexes, said first conjugate comprising a composition comprising an anti-IgM monoclonal or polyclonal antibody attached to a signal-generating compound capable of generating a detectable signal and said second conjugate comprising a composition comprising an anti-IgG monoclonal or polyclonal antibody attached to a signal-generating compound capable of generating a detectable signal; and (d) detecting IgM and IgG antibodies which may be present in said test sample by detecting a signal generated by said signal-generating compounds.

ANSWER 9 OF 10 USPATFULL on STN

94:110663 Monoclonal antibody for differentiating HIV-2 from HIM-1 seropositive individuals.

Hunt, Jeffrey C., Lindenhurst, IL, United States Sarin, Virender K., Libertyville, IL, United States Devare, Sushil G., Northbrook, IL, United States Tribby, Ilse I. E., Chicago, IL, United States Desai, Suresh M., Libertyville, IL, United States Casey, James M., Gurnee, IL, United States Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation) US 5374518 19941220 APPLICATION: US 1992-952482 19920928 (7) DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

What is claimed is:

- 1. A monoclonal antibody which recognizes an epitope of a HIV-2 qp41 antigen comprising the amino acid sequence HTTVPW but which does not bind to HIV-1, and whose binding to said epitope depends on the binding of the antigen combining site of the antibody to the amino acid residues present in the amino acid sequence HTTVPW.
- 2. The monoclonal **antibody** of claim 1 produced by ATCC Deposit No. HB 10012.
- 3. A hybridoma cell line producing a monoclonal antibody which recognizes an epitope of a HIV-2 gp41 antigen comprising the amino acid sequence HTTVPW but which does not bind to HIV-1, and whose binding to said epitope depends on the binding of the antigen combining site of the antibody to the amino acid residues present in the amino acid sequence HTTVPW.
- 4. The hybridoma cell line of claim 3, wherein said cell line is ATCC Deposit No. HB 10012.
- 5. A peptide, consisting of an amino acid sequence HTTVPW which specifically binds antibody to HIV-2 but which does not bind antibody to HIV-1.
- 6. A competitive assay for differentiating HIV-2 infection from HIV-1 infection, comprising the steps of: a. contacting a biological sample with (i) a monoclonal antibody, which recognizes an epitope of a HIV-2 gp41 antigen comprising the amino acid sequence HTTVPW but which does not bind to HIV-1, and whose binding to said epitope depends on the binding of the antigen combining site of the antibody to the amino acid residues present in the amino acid sequence HTTVPW, and (ii) with a solid phase to which has been attached a recombinant or native HIV-2 gp41 protein containing said sequence, thereby forming a mixture; b. incubating said mixture for a time and under conditions sufficient to form complexes of monoclonal antibody/solid phase and/or biological sample/solid phase; and c. determining the amount of monoclonal antibody bound to said solid phase as an indication of exposure to HIV-2.
- 7. The method of claim 6, wherein said monoclonal antibody is produced by ATCC Deposit No. HB 10012.
- 8. The method of claim 6, wherein said monoclonal antibody is labeled

9. A method for detecting HIV-2 infection comprising reacting a test sample with one or more reagents selected from the group consisting of (i) a monoclonal **antibody**, which recognizes an epitope of a HIV-2 gp41 antigen comprising the amino acid sequence HTTVPW but which does not bind to HIV-1, and whose binding to said epitope depends on the binding of the antigen combining site of the **antibody** to "said" the amino acid residues present in the amino acid sequence HTTVPW, and (ii) an antigen comprising the amino acid sequence HTTVPW which specifically binds to HIV-2 but which does not bind to HIV-1.

- 10. A method for determining the presence of **antibody** to HIV-2 gp41 in a biological sample, comprising the steps of: a. contacting the sample with an antigen consisting of the amino acid sequence HTTVPW, whereby an antigen/antibody complex is formed; and b. determining the amount of said complex formed as an indication of the presence of **antibody** to HIV-2 gp41 in the sample.
- 11. A kit for use in detecting exposure of an individual to HIV-2, comprising a container of monoclonal **antibody** which recognizes an epitope of a HIV-2 gp41 antigen comprising the amino acid sequence HTTVPW but which does not bind to HIV-1, and whose binding to said epitope depends on the binding of the antigen combining site of the **antibody** to the amino acid residues present in the amino acid sequence HTTVPW.
- 12. A kit for use in detecting exposure of an individual to HIV-2, comprising a container of immobilized antigen which specifically binds **antibody** to HIV-2 gp41 but which does not bind **antibody** to HIV-1, wherein said antigen consists of the amino acid sequence HTTVPW.
- L5 ANSWER 10 OF 10 USPATFULL on STN
- 92:104887 Mouse monoclonal **antibodies** to hiv-1p24 and their use in diagnostic tests.

Mehta, Smriti U., Libertyville, IL, United States

Hunt, Jeffrey C., Lindenhurst, IL, United States

Devare, Sushil G., Northbrook, IL, United States

Devare, Sushil G., Northbrook, IL, United States

Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation) US 5173399 19921222

APPLICATION: US 1988-204798 19880610 (7) DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. An immunoassay for the detection of HIV-I p24 antigen in a test sample comprising forming an **antibody**/antigen complex wherein the **antibody** portion of said complex comprises a mixture of murine monoclonal **antibodies**, at least one monoclonal **antibody** of said mixture being capable of specifically binding to an epitope on HIV-I p24 to which epitope human anti-HIV-I p24 lgG does not competitively bind, and at least one other monoclonal **antibody** of said mixture being capable of binding to a different epitope of HIV-I p24 to which different epitope human anti-HIV-I p24 lgG competitively binds, and detecting the presence or amount in picogram sensitivity of the **antibody**/antigen complex formed.
- 2. The immunoassay of claim 1 wherein the presence or amount of the **antibody**/antigen complex formed is determined by incubating said complex with a labelled, anti-species **antibody** specific for said monoclonal **antibodies**.
- 3. The immunoassay of claim 2 wherein said label comprises a radioisotope, enzyme, fluorescent compound, chemiluminescent compound, or member of a specific binding pair.
- 4. The immunoassay of claim 1 wherein the **antibody** which binds to the epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind is monoclonal **antibody** 31-42-19 and the **antibody** which binds to the different epitope to which different epitope human anti-HIV-1 p24 IgG competitively binds is monoclonal **antibody** 31-90-25.
- 5. The immunoassay of claim 4 wherein said monoclonal **antibodies** 31-42-19 and 31-90-25 are in solution.
- 6. The immunoassay of claim 4 wherein said monoclonal  ${\tt antibodies}$  31-42-19 and 31-90-25 are coated on a solid support.
- 7. The immunoassay of claim 5 wherein said **antibody** portion of said complex further comprises human anti-HIV-I IgG coated on a solid support.
- 8. The immunoassay of claim 6 wherein said antibody portion of said

- 9. The immunoassay of claim 8 wherein said antibody portion of said complex further comprises anti-HIV-I  $F(ab')_2$ .
- 10. The immunoassay of claim 9 wherein said antibody portion of said complex further comprises anti-HIV-I p24 F(ab')<sub>2</sub>.
- 11. A diagnostic reagent for detection of HIV-1 p24 antigen or HIV-2 p24 antigen comprising a monoclonal **antibody** which specifically binds to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind and which monoclonal **antibody** also specifically binds to HIV-2 p24.
- 12. An immunoassay for the detection of HIV-1 p24 antigen in a human test sample comprising: a. contacting a human test sample with a solid support coated with human anti-HIV-1 IgG for a time and under conditions sufficient to form antibody/antigen complexes; b. contacting said complexes with a murine monoclonal antibody mixture comprising monoclonal antibodies 31-42-19 secreted by ATCC HB 9726 and 31-90-25 secreted by ATCC HB 9725 for a time and under conditions sufficient to form antibody/antigen/antibody complexes; c. contacting said antibody/antigen/antibody complexes with an anti-mouse antibody or fragment thereof conjugated to a detectable label capable of generating a measurable signal; d. measuring the signal generated to determine the presence of HIV-1 p24 in picogram sensitivity in the test sample.
- 13. The immunoassay of claim 12 wherein said solid support is simultaneously contacted with said human test sample and said mouse monoclonal  ${f antibody}$  mixture.
- 14. An immunoassay for detection of the presence or amount of HIV-2 p24 antigen in a human test sample, comprising forming an **antibody**/antigen complex wherein the **antibody** portion of said complex comprises a monoclonal **antibody** capable of specifically binding to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind and which monoclonal **antibody** also specifically binds to HIV-2 p24, and detecting the presence or amount of the **antibody**/antigen complex formed.
- 15. A diagnostic kit for the detection of HIV-1 p24 antigen comprising: a container containing a mixture of at least two murine monoclonal **antibodies** wherein at least one monoclonal **antibody** of said mixture specifically binds to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind and wherein at least one other monoclonal **antibody** of said mixture specifically binds to a different epitope of HIV-1 p24 to which different epitope human anti-HIV-1 p24 IgG competitively binds.
- 16. The diagnostic kit of claim 15 wherein said murine monoclonal **antibody** which specifically binds to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind is designated as monoclonal **antibody** 31-42-19 secreted by the hybridoma cell line ATCC 9726 and wherein said monoclonal **antibody** which is capable of binding to a different epitope of HIV-1 p24 to which different epitope human anti-HIV-1 p24 IgG competitively binds is designated as the 31-90-25 monoclonal **antibody** secreted by the hybridoma cell line ATCC HB 9725.
- 17. The immunoassay of claim 12 wherein said solid support is selected from the group consisting of wells of reaction trays, test tubes, polystyrene beads, strips, membranes and microparticles.
- 18. The immunoassay of claim 12 wherein said label is selected from the group consisting of enzymes, radioisotopes, fluorescent compounds and chemiluminescent compounds.
- 19. The immunoassay of claim 18 wherein said enzymatic label is horseradish peroxidase.
- 20. The immunoassay of claim 12, 18 or 19 further comprising a hapten and labelled anti-hapten system wherein the hapten is conjugated to the labeled murine monoclonal **antibody**.
- 21. The diagnostic reagent of claim 20 wherein said monoclonal **antibody** is the monoclonal **antibody** secreted by the hybridoma cell line A.T.C.C. HB 9726.

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     HUNT, J C; KONRATH, J G; LOU, S C; QIU, X; SCHEFFEL, J W; TYNER, J D
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L13 ANSWER 5 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

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     B04 D16
TN
     HUNT, J C; KONRATH, J G; LOU, S C; QIU, X; SCHEFFEL, J W; TYNER, J D
     (HUNT-I) HUNT J C; (KONR-I) KONRATH J G; (LOUS-I) LOU S C; (QIUX-I) QIU X;
     (SCHE-I) SCHEFFEL J W; (TYNE-I) TYNER J D
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L13 ANSWER 7 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
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     2005-202217 [21]; 2005-202218 [21]; 2005-232160 [24]
DNC C2004-149486
     New monoclonal antibody that binds to a shared epitope of Human
     {\tt Immunodeficiency\ Virus-1\ protein\ p24\ and\ Human\ Immunodeficiency\ Virus-2}
     protein p26, useful in preparing a composition for diagnosing or treating
     AIDS.
DC
     B04 D16
     HUNT, J C; KONRATH, J G; LOU, S C; QIU, X; SCHEFFEL, J W; TYNER, J D
IN
     (HUNT-I) HUNT J C; (KONR-I) KONRATH J G; (LOUS-I) LOU S C; (QIUX-I) QIU X;
     (SCHE-I) SCHEFFEL J W; (TYNE-I) TYNER J D
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ADT US 2004101831 A1 Div ex US 2000-731126 20001206, US 2003-714689 20031117
PRAI US 2000-731126
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L13 ANSWER 8 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
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    C2002-197524
    New monoclonal antibody which binds to a shared epitope of human
     immunodeficiency virus (HIV)-1 protein p24 and HIV-2 protein p26, useful
     for detecting presence of HIV antigens.
DC
     B04 D16
    HUNT, J C; KONRATH, J G; LOU, S C; QIU, X; SCHEFFEL, J W; TYNER, J D
IN
     (ABBO) ABBOTT LAB; (HUNT-I) HUNT J C; (KONR-I) KONRATH J G; (LOUS-I) LOU S
     C; (QIUX-I) QIU X; (SCHE-I) SCHEFFEL J W; (TYNE-I) TYNER J D
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                   W 20041209 (200481)
    JP 2004536568
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   US 2002106636 A1 US 2000-731126 20001206; WO 2002064615 A2 WO 2001-US43179
    20011205; EP 1341820 A2 EP 2001-273730 20011205, WO 2001-US43179 20011205;
    US 6818392 B2 US 2000-731126 20001206; JP 2004536568 W WO 2001-US43179
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L17 ANSWER 1 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI New monoclonal **antibody** used for detecting a marker indicative of exposure to human immunodeficiency virus (**HIV**) I in a sample by forming

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L17 ANSWER 2 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
    Mouse monoclonal antibody detecting HIV-2 seropositive individuals -
     is specific for epitope of HIV-2 GP 41 and recognised by monoclonal
      antibody of amino acid sequence HT TV PW.
L17 ANSWER 3 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
     New monoclonal antibodies recognising HIV p24 antigen - providing very
     sensitive detection before patients are sero positive for antibodies.
L17 ANSWER 4 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
     Monoclonal antibody of HIV I gP41 epitope - used for producing a
     highly specific reagent for detecting prior exposure to HIV.
=> d 117,bib,1-4
L17 ANSWER 1 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
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    New monoclonal antibody used for detecting a marker indicative of
     exposure to human immunodeficiency virus (HIV) I in a sample by forming
     an antibody/antigen complex.
DC:
     B04 D16
     DAWSON, G J; DEVARE, S G; FALK, L A; HUNT, J C; SARIN, V K; WEBBER, J S;
     WRAY, L K
     (DAWS-I) DAWSON G J; (DEVA-I) DEVARE S G; (FALK-I) FALK L A; (HUNT-I) HUNT
PA
     J C; (SARI-I) SARIN V K; (WEBB-I) WEBBER J S; (WRAY-I) WRAY L K
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     US 2003118985 A1 20030626 (200379)*
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PRAI US 1997-856155
                          19970514; US 2001-86409
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L17 ANSWER 2 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
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     Mouse monoclonal antibody detecting HIV-2 seropositive individuals -
     is specific for epitope of HIV-2 GP 41 and recognised by monoclonal
     antibody of amino acid sequence HT TV PW.
DC
     B04 D16 S03
     CASEY, J M; DESAI, S M; DEVARE, S G; HUNT, J C; JOHNSON-PAEPKE, J; SARIN, V K; TRIBBY, I I E; JOHSNONPAE, J
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     ES 2066887
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     388602 B1 EP 1990-101860 19900131; DE 69013950 E DE 1990-613950 19900131.
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FDT AU 646460 B Previous Publ. AU 9177117; DE 69013950 E Based on EP 388602;
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L17 ANSWER 3 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
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    DEVARE, S G; HUNT, J C; MEHTA, S U
PA
     (ABBO) ABBOTT LAB
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     CA 1340919
                     C 20000307 (200031)
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    EP 345461 A EP 1989-108001 19890503; JP 02107196 A JP 1989-132515
     19890525; US 5173399 A US 1988-204798 19880610; EP 345461 B1 EP
     1989-108001 19890503; DE 68918497 E DE 1989-618497 19890503, EP
     1989-108001 19890503; ES 2065935 T3 EP 1989-108001 19890503; CA 1340919 C
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L17 ANSWER 4 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
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     DAWSON, G J; DEVARE, S G; FALK, L A; HUNT, J C; SARIN, V K; WEBBER, J S;
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               E SCHEFFEL JAMES W/IN
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            8 L21 AND (HIV)
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    B04 D16 S03
IN
    MOORE, B S; SCHEFFEL, J W
    (ABBO) ABBOTT LAB
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WO 2000026673 A1 20000511 (200031)* EN
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                        DNC C2000-053354
    Novel monoclonal antibodies useful as positive control reagent for
     detecting human immunodeficiency virus infections and diagnosing,
     evaluating or prognosing viral disease.
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 IN
     HACKETT, J R; HICKMAN, R K; SCHEFFEL, J W; TYNER, J D
PΑ
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L26 ANSWER 3 OF 3 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
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AN
DNN N1997-089946
                       DNC C1997-034622
    Detection of antibodies to hepatitis C virus - using recombinant
     polypeptide prepd. by expression of E2 truncated protein, rabbit heavy
     chain signal sequence and human pro-urokinase.
     B04 D16 S03
     LESNIEWSKI, R R; OKASINSKI, G F; SCHAEFER, V G; SCHEFFEL, J W; SUHAR, T S
IN
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ADT WO 9641196 A1 WO 1996-US8536 19960604; EP 836708 A1 EP 1996-917969
     19960604, WO 1996-US8536 19960604; JP 11507129 W WO 1996-US8536 19960604,
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L30 ANSWER 1 OF 1 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2000-171290 [15]
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                      DNC C2000-053354
TI Novel monoclonal antibodies useful as positive control reagent for
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evaluating or prognosing viral disease.
     B04 D16 S03
ΤN
    HACKETT, J R; HICKMAN, R K; SCHEFFEL, J W; TYNER, J D
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On December 11, 2005, the 2006 MeSH terms were loaded.
The MEDLINE reload for 2006 is now (26 Feb.) available. For details
on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:
   http://www.nlm.nih.gov/mesh/
   http://www.nlm.nih.gov/pubs/techbull/nd04/nd04 mesh.html
   http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
   http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html
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MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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- · L31 ANSWER 1 OF 7 MEDLINE on STN
- TI Seven human immunodeficiency virus (HIV) antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection.
- L31 ANSWER 2 OF 7 MEDLINE on STN
- TI Antienvelope antibodies are protective against GBV-C reinfection: evidence from the liver transplant model.
- L31 ANSWER 3 OF 7 MEDLINE on STN
- TI Antibodies against the GB virus C envelope 2 protein before liver transplantation protect against GB virus C de novo infection.
- L31 ANSWER 4 OF 7 MEDLINE on STN
- TI Antibody to GBV-C second envelope glycoprotein (anti-GBV-C E2): is it a marker for immunity?.
- L31 ANSWER 5 OF 7 MEDLINE on STN
- TI One-step competitive immunochromatographic assay for semiquantitative determination of lipoprotein(a) in plasma.
- L31 ANSWER 6 OF 7 MEDLINE on STN
- TI Nucleotide sequence of messenger RNA encoding VHDJH and VKJK of a highly

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L31 ANSWER 7 OF 7 MEDLINE on STN

TI Studies on the biosynthesis of riboflavin by Ashbya gossypii. III.

Comparison of the utilization of glucose and maltose by Ashbya gossypii.

=> d 131,cbib,ab

L31 ANSWER 1 OF 7 MEDLINE on STN
2001482949. PubMed ID: 11526139. Seven human immunodeficiency virus (HIV) antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection. Ly T D: Martin I: Daghfal D: Goodwidge
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2001482949. PubMed ID: 11526139. Seven human immunodeficiency virus (HIV) antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection. Ly T D; Martin L; Daghfal D; Sandridge A; West D; Bristow R; Chalouas L; Qiu X; Lou S C; Hunt J C; Schochetman G; Devare S G. (Laboratoire Claude Levy, Ivry sur Seine, France. ) Journal of clinical microbiology, (2001 Sep) Vol. 39, No. 9, pp. 3122-8. Journal code: 7505564. ISSN: 0095-1137. Pub. country: United States. Language: English.

In this study, we evaluated the performance of two prototype human ΆR immunodeficiency virus (HIV) antigen-antibody (Ag-Ab) combination assays, one from Abbott Laboratories (AxSYM HIV Ag-Ab) and the other from  ${\tt bioMerieux} \ \ ({\tt VIDAS} \ {\tt HIV} \ {\tt Duo} \ \ {\tt Ultra}) \, , \ {\tt versus} \ \ {\tt five} \ \ {\tt combination} \ \ {\tt assays}$ commercially available in Europe. The assays were Enzygnost HIV Integral, Genscreen Plus HIV Ag-Ab, Murex HIV Ag-Ab Combination, VIDAS HIV Duo, and Vironostika HIV Uniform II Ag-Ab. All assays were evaluated for the ability to detect p24 antigen from HIV-1 groups M and O, antibody-positive plasma samples from HIV-1 groups M and O, HIV-2, and 19 HIV seroconversion panels. Results indicate that although all combination assays can detect antibodies to HIV-1, group M, subtypes A to G, circulating recombinant form (CRF) A/E, and HIV-1 group O, their sensitivity varied considerably when tested using diluted HIV-1 group O and HIV-2 antibody-positive samples. Among combination assays, the AxSYM, Murex, and VIDAS HIV Duo Ultra assays exhibited the best antigen sensitivity (at approximately 25 pg of HIV Ag/ml) for detection of HIV-1 group M, subtypes A to G and CRF A/E, and HIV-1 group O isolates. However, the VIDAS HIV Duo Ultra assay had a lower sensitivity for HIV-1 group M and subtype C, and was unable to detect subtype C antigen even at 125 pg of HIV Ag/ml. The HIV antigen sensitivity of the VIDAS HIV Duo and Genscreen Plus combination assays was approximately 125 pg of HIV Ag/ml for detection of all HIV-1 group M isolates except HIV-1 group O while the sensitivity of Vironostika HIV Uniform II Ag-Ab and Enzygnost HIV Integral Ag-Ab assays for all the group M subtypes was >125 pg of HIV Ag/ml. Among the combination assays, the AxSYM assay had the best performance for detection of early seroconversion samples, followed by the Murex and VIDAS HIV Duo Ultra assays.

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=> d 135, ti, 1-9
L35 ANSWER 1 OF 9
                       MEDLINE on STN
     Multicenter evaluation of a new, automated enzyme-linked immunoassay for
     detection of human immunodeficiency virus-specific \ensuremath{\mathsf{antibodies}} and
     antigen.
L35 ANSWER 2 OF 9
                      MEDLINE on STN
     Envelope sequence variability and serologic characterization of HIV type
     1 group O isolates from equatorial guinea.
L35 ANSWER 3 OF 9
                       MEDLINE on STN
     Molecular analyses of HIV-1 group O and HIV-2 variants from Africa.
                       MEDLINE on STN
L35 ANSWER 4 OF 9
     Discrimination between HIV-1 and HIV-2-seropositive individuals using
     mouse monoclonal antibodies directed to HIV transmembrane proteins.
                       MEDLINE on STN
     Diagnostic utility of a mouse monoclonal antibody (5-21-3) employed as a
     competitive probe in an immunoassay to detect antibody to HIV-1 gp41.
L35 ANSWER 6 OF 9
                       MEDLINE on STN
     Mouse monoclonal antibody 5-21-3 recognizes a contiguous,
     conformation-dependent epitope and maps to a hydrophilic region in {f HIV}-1
     gp41.
L35 ANSWER 7 OF 9
                       MEDLINE on STN
    Prevalence of antibodies to the core protein P17, a serological marker
     during HIV-1 infection.
L35 ANSWER 8 OF 9
                       MEDLINE on STN
TI Genes of human immunodeficiency virus, type I (HIV-I), their expression
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L35 ANSWER 9 OF 9 MEDLINE on STN

TI Reliable detection of individuals seropositive for the human immunodeficiency virus (HIV) by competitive immunoassays using Escherichia coli-expressed HIV structural proteins.

=> d 135,cbib,ab,1-9

L35 ANSWER 1 OF 9 MEDLINE on STN

2004018747. PubMed ID: 14715727. Multicenter evaluation of a new,
automated enzyme-linked immunoassay for detection of human
immunodeficiency virus-specific antibodies and antigen. Sickinger Eva;
Stieler Myriam; Kaufman Boris; Kapprell Hans-Peter; West Daniel; Sandridge
Arnold; Devare Sushil; Schochetman Gerald; Runt J C; Daghfal David.
(Abbott Diagnostika GmbH & Co KG, Wiesbaden, Germany. (AxSYM Clinical
Study Group). ) Journal of clinical microbiology, (2004 Jan) Vol. 42, No.
1, pp. 21-9. Journal code: 7505564. ISSN: 0095-1137. Pub. country: United
States. Language: English.

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A collaborative multicenter study was conducted to evaluate the sensitivity, specificity, and precision of a three-step, fully automated, qualitative microparticle-based enzyme-linked immunoassay (AxSYM HIV Ag/Ab Combo; Abbott Laboratories), designed to simultaneously detect (i). antibodies against human immunodeficiency virus type 1 (HIV-1) and/or type 2 (HIV-2) and (ii). HIV p24 antigen. A significant reduction in the HIV seroconversion window was achieved by combining detection of HIV antibodies and antigen into a single assay format. For 22 selected, commercial  $\boldsymbol{\mathtt{HIV}}$  seroconversion panels, the mean time of detection with the combined-format HIV antigen-antibody assay was reduced by 6.15 days compared to that with a similar third-generation single-format HIV antibody assay. The quantitative sensitivity of the combination assay for the p24 antigen (17.5 pg/ml by use of the p24 quantitative panel VIH SFTS96') was nearly equivalent to that of single-format antigen tests. The combination assay demonstrated sensitive (100%) detection of anti-HIV immunoglobulin in specimens from individuals in CDC stages A, B, and C and from individuals infected with different HIV-1 group M subtypes, group O, or HIV-2. The apparent specificity for hospitalized patients (n = 1938) was 99.90%. In a random population of 7900 volunteer blood donors, the specificity (99.87%) was comparable to that of a third-generation single-format HIV antibody assay (99.92%) on the same donor specimens. In addition, the combination assay was robust to potential interfering specimens. The precision of the combination was high, with intra- and interrun variances of <or=9.3% for each precision panel specimen or assay control and <or=5.3% for the negative assay control.

L35 ANSWER 2 OF 9 MEDLINE on STN
97407537. PubMed ID: 9264286. Envelope sequence variability and serologic characterization of HIV type 1 group O isolates from equatorial guinea.

Hunt J C; Golden A M; Lund J K; Gurtler L G; Zekeng L; Obiang J; Kaptue L; Hampl H; Vallari A; Devare S G. (AIDS Research and Retrovirus Discovery, Abbott Laboratories, North Chicago, Illinois 60064, USA. ) AIDS research and human retroviruses, (1997 Aug 10) Vol. 13, No. 12, pp. 995-1005. Journal code: 8709376. ISSN: 0889-2229.

Report No.: PIP-129455; POP-00272760. Pub. country: United States. Language: English.

Four sera from Equatorial Guinea (EG) suspected to contain antibody against HIV-1 group O-related viruses were identified on the basis of unusual and differential serologic reactivity in selected commercial assays and Western blot. Degenerate primers, designed from HIV-1 group O published sequences, were used to PCR amplify envelope (env) gene sequences from the suspect EG sera. A complete envelope gene sequence from each serum was determined from the overlapping env gene fragments. Analysis (PHYLIP package of programs) of Env amino acid sequences (translated from nucleotide sequences) indicated that the amino acid sequences obtained from EG sera clustered more closely with HIV Env sequences of group O compared to group M. The amino acid sequences at the octameric tip of the V3 loop were either RIGPLAWY (one isolate), RIGPMAWY (two isolates), or GLGPLAVY (one isolate). The V3 tip tetrameric sequence GPLA is represented only once in the 1995 HIV (Los Alamos) database, but was present in two of our group O-related EG samples. The gp41 immunodominant regions (IDR) protein sequences were identical for sequences from three of the sera, RLLALETLIQNQQLLNLWGCKGR(K)L(I)VCYTSVK(T) W, whereas sequence from the fourth serum contained three changes as noted in parentheses. IDR sequences derived from EG sera were unique compared to those reported for other HIV-1 group O isolate ANT70, VAU, or MVP5180. Antibody in each EG serum directed against the IDR could be detected using synthetic peptides comprising sequences from the ANT70 or MVP5180 IDRs, but were most reactive against the sequences derived from the samples themselves. Little or no serologic reactivity was detected when EG sera were reacted against peptides comprising the IDR of  $\boldsymbol{\mathtt{HIV}}{-}1$ group M (subtype B consensus) or **HIV-**2 (consensus). The genetic

. warranton and opinimizatog; or ma. a group o routanno are or committeening importance to the design of HIV-1 diagnostic and screening assays, especially since current serologic and genetic methods to detect HIV-1 have been developed mainly on the basis of sequences from isolates belonging to HIV-1 group M. The HIV envelope protein, especially the gp41 immunodominant region, plays a major antigenic role in the detection of HIV infection and for discriminating HIV-1 from HIV-2 antibody. This paper reports upon genetic variation and the serologic characterization of env sequences from 4 people living in Equatorial Guinea (EG) who were infected with HIV-1 group O. Selected commercial assays and Western blot were first used to identify the sera, then degenerate primers, designed from HIV-1 group O published sequences, were used to PCR amplify envelope (env) gene sequences. A complete envelope gene sequence from each serum was determined from the overlapping env gene fragments. The env amino acid sequence analysis found the EG sera sequences to be clustered more closely with the  ${f HIV}$  env sequences of group O rather than to group M. The amino acid sequences at the octameric tip of the V3 loop were either RIGPLAWY, RIGPMAWY, or GLGPLAVY. Although the V3 tip tetrameric sequence GPLA is represented only once in the 1995 HIV database, it was present in 2 of the group O-related EG samples. The gp41 immunodominant regions (IDR) protein sequences were identical for sequences from 3 of the sera. IDR sequences derived from the EG sera were unique compared to those reported for other HIV-1 group O isolates ANT70, VAU, or MVP5180. Other findings are discussed in detail.

- L35 ANSWER 3 OF 9 MEDLINE on STN
- 97353064. PubMed ID: 9209322. Molecular analyses of HIV-1 group O and HIV-2 variants from Africa. Hunt J C; Brennan C A; Golden A M; Yamaguchi J; Lund J K; Vallari A S; Hickman R K; Zekeng L; Gurtler L G; Hampl H; Kaptue L; Devare S G. (Abbott Laboratories, North Chicago, IL-60064, USA.) Leukemia: official journal of the Leukemia Society of America, Leukemia Research Fund, U.K, (1997 Apr) Vol. 11 Suppl 3, pp. 138-41. Journal code: 8704895. ISSN: 0887-6924. Pub. country: ENGLAND: United Kingdom. Language: English.
- Genetic variation among HIV isolates creates challenges for their detection by serologic and genetic techniques. To characterize the sequence variation and its correlation to serologic diversity of HIV-1 Group O and HIV-2 isolates, samples were identified by differential reactivity in selected commercial and research assays. Analysis of sera from Equatorial Guinea (EG) led to identification of 4 HIV-1 Group O variants. Viral RNA, extracted from these samples was used to PCR amplify overlapping sequences of the entire envelope gene using multiple primer pairs. Sequence analysis indicated that the V3 loop nucleotide and protein sequences aligned more closely with HIVANT70 compared to other Group O sequences. The amino acid sequences at the octameric tip of the V3 loop were RIGPLAWY, RIGPMAWY, or GLGPLAVY. The tetrameric tip GPLA is represented only once in the published 1994 HIV database (Los Alamos) but was present in 2 of 4 of EG samples. The immuno-dominant region (IDR) sequences derived from EG sera were unique in that none of the sequences were completely homologous to other HIV-1 group O variants. Further, the HIV-1 group O sequence variation could be correlated with differential serologic reactivity using IDR peptides. Compared to HIV-1, the sequence information on HIV-2 isolates is relatively limited, though the  ${\tt HIV-2}$  isolates also show genetic variation similar to HIV-1. To further establish a correlation between the genetic diversity and serologic detection of HIV-2, plasma samples from Western Africa were evaluated. Eight samples were selected based on weak serologic reactivity to env proteins. PCR amplification and sequence analysis of the gag, env V3 loop, and env IDR regions indicated that the samples could be classified as subtypes A (4 samples), B (3 samples) and D (1 sample). Across the subtypes, there was conservation in the IDR region of the sequence WGCAFRQVCHT. This region is absolutely conserved among the majority of currently known HIV-2 and related SIV viruses (1994 HIV database). One subtype B sample had a unique sequence immediately adjacent to the IDR, however, this did not change the serologic detection using a HIV-2 IDR specific monoclonal antibody.
- L35 ANSWER 4 OF 9 MEDLINE on STN 90359273. PubMed ID: 2202352. Discrimination between HIV-1 and HIV-2-seropositive individuals using mouse monoclonal antibodies directed to HIV transmembrane proteins. Hunt J C; Johnson-Paepke J; Boardway K; Gutierrez R; Hampl H; Allen R; Heynen C; Desai S; Casey J; Tribby I; +. (Department of Human Retroviruses, Abbott Diagnostics Division, Abbott Laboratories, Abbott Park, IL 60064. ) AIDS research and human retroviruses, (1990 Jul) Vol. 6, No. 7, pp. 883-98. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English. Mouse monoclonal antibodies directed against the transmembrane proteins of HIV-1 or HIV-2 provided site-directed, unambiguous discrimination between HIV-1 and HIV-2 antibody-positive sera, when employed in immunoassays as competitive probes against serum antibodies. These monoclonal antibodies mapped to epitopes outside of the

well-characterized immunodominant regions (IDR) of the transmembrane

processes. The memorial compositions themshoused has a superior meetica for discrimination compared with immunoprecipitation of metabolically radiolabeled HIV envelope glycoproteins, Western blot against viral envelope glycoproteins, or noncompetitive enzyme immunoassays employing HIV recombinant transmembrane proteins or synthetic IDR peptides as serological targets. The monoclonal competitive assay was not affected by antigenic cross reactivity or nonspecific reactivity exhibited by selected serum samples toward envelope proteins or peptides, respectively. Results of the monoclonal competitive immunoassay were supported by results of a peptide inhibition assay employing free IDR peptides in competition with IDR peptides on a solid support for binding of serum antibody. IDR peptide inhibition clearly demonstrated non-cross-reactive antigenic specificity of sera toward either the HIV-1 IDR or the HIV-2 IDR. The monoclonal competitive assay also identified samples containing antibody to both HIV-1 and HIV-2 transmembrane proteins. Analysis of these samples by IDR peptide inhibition indicated they contained two distinct, non-cross-reactive populations of antibodies, one directed to the  ${\tt HIV-1}$  IDR and the other directed to the  ${\tt HIV-2}$  IDR.

- L35 ANSWER 5 OF 9 MEDLINE on STN 90298076. PubMed ID: 1694452. Diagnostic utility of a mouse monoclonal antibody (5-21-3) employed as a competitive probe in an immunoassay to detect antibody to HIV-1 gp41. Hunt J C; Falk L; Webber J S; Decker R H; Devare S G; Dawson G J. (Department of Human Retroviruses, Abbott Laboratories, North Chicago, Illinois 60064. ) AIDS research and human retroviruses, (1990 May) Vol. 6, No. 5, pp. 599-606. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English. A mouse monoclonal antibody, designated 5-21-3, was raised against HIV-1 gp41 using detergent-disrupted virus as the immunogen. Antibody 5-21-3 was conjugated to horseradish peroxidase (HRP) and employed as a competitive probe against normal and HIV-1 antibody-positive sera in an immunoassay to detect the presence of antibody to HIV-1 gp41. The diagnostic utility of the competitive monoclonal immunoassay was assessed by correlation to a similar assay which employed HRP-labeled polyclonal IgG from a gp41-seropositive donor as the competitive probe. The monoclonal immunoassay was greater than 98% as sensitive and 99% as specific as the polyclonal immunoassay, regardless of the geographic source or disease state of the donor. The monoclonal immunoassay also was nearly as effective as the polyclonal immunoassay in detecting points of seroconversion in individuals enrolled in longitudinal studies. Of
- L35 ANSWER 6 OF 9 MEDLINE on STN 90298075. PubMed ID: 1694451. Mouse monoclonal antibody 5-21-3 recognizes a contiguous, conformation-dependent epitope and maps to a hydrophilic region in HIV-1 gp41. Hunt J C; Desai S M; Casey J M; Bolling T J; Leung T K; Decker R H; Devare S G; Sarin V. (Department of Human Retroviruses, Abbott Laboratories, Abbott Park, Illinois 60064.) AIDS research and human retroviruses, (1990 May) Vol. 6, No. 5, pp. 587-98. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

particular interest was the finding that the epitope recognized by monoclonal antibody 5-21-3 did not map to the well-characterized gp41

immunodominant region.

- Mouse monoclonal antibody 5-21-3 is mapped to an epitope within a hydrophilic region of HIV-1 gp41 between amino acids 642 and 665 (numbering by Meyers et al. based on HXB2 isolate). The epitope is formed from amino acids within the sequence IHSLIEESQNQQEKNEQELLELDK; however, antibody 5-21-3 is unable to recognize the epitope-forming sequence when it is presented to the antibody in the form of a short (642-665) synthetic polypeptide. The epitope apparently is partially formed when additional native sequence of varying length is added to the amino and/or carboxy ends of the epitope-forming sequence, and 5-21-3 binds these larger synthetic polypeptides to varying degrees depending on the position and length of the flanking sequences. The 5-21-3 epitope apparently is formed from contiguous amino acids which require a specific, conformation-dependent, secondary structure for proper epitope formation. Binding preferences exhibited by 5-21-3 toward synthetic polypeptides and recombinant proteins may reflect the conformational nature of the epitope in disrupted HIV which elicited formation of the monoclonal.
- L35 ANSWER 7 OF 9 MEDLINE on STN
  90253933. PubMed ID: 1692727. Prevalence of antibodies to the core
  protein P17, a serological marker during HIV-1 infection. Mehta S U;
  Rupprecht K R; Hunt J C; Kramer D E; McRae B J; Allen R G; Dawson G J;
  Devare S G. (Human Retroviruses Department, Abbott Laboratories, Abbott
  Park, IL.) AIDS research and human retroviruses, (1990 Apr) Vol. 6, No.
  4, pp. 443-54. Journal code: 8709376. ISSN: 0889-2229. Pub. country:
  United States. Language: English.
- AB Studies on monitoring the immune response to viral structural proteins during human immunodeficiency virus (HIV-1) infection have established the significance of antibodies to the core protein p24 during the progression of the disease. We have studied the prevalence of antibodies to the core protein p17 in order to study their diagnostic

HIV-1 p17, molecularly cloned and expressed in Escherichia coli was purified by immunoaffinity chromatography using an HIV-1 p17-specific monoclonal antibody. A highly sensitive enzyme-linked immunoassay was developed using the purified recombinant p17 as the serological target to detect antibodies to p17. The results indicated that antibodies to p17 decline during progression of disease, with the decline being more dramatic as patients moved from asymptomatic to AIDS-related complex (ARC). Patient specimens deficient in p24 antibody, but having detectable levels of antibody to p17 were almost always positive for p24 antigen. Under these conditions, p17 antibody is an important serological marker because it provides a more consistent marker for core antigens during HIV-1 infection.

L35 ANSWER 8 OF 9 MEDLINE on STN
89358037. PubMed ID: 3076578. Genes of human immunodeficiency virus, type
I (HIV-I), their expression in Escherichia coli, and their utility in
diagnosis of virus infection. Devare S G; Desai S M; Rupprecht K R; Allen
R G; Dawson G J; Hunt J C; Casey J M. Indian journal of biochemistry &
biophysics, (1988 Dec) Vol. 25, No. 6, pp. 504-9. Journal code: 0310774.
ISSN: 0301-1208. Pub. country: India. Language: English.

L35 ANSWER 9 OF 9 MEDLINE on STN
88088991. PubMed ID: 3275722. Reliable detection of individuals
seropositive for the human immunodeficiency virus (HIV) by competitive
immunoassays using Escherichia coli-expressed HIV structural proteins.
Dawson G J; Heller J S; Wood C A; Gutierrez R A; Webber J S; Hunt J C;
Hojvat S A; Senn D; Devare S G; Decker R H. (Hepatitis/AIDS Research
Department, Abbott Laboratories, North Chicago, Illinois 60064.) The
Journal of infectious diseases, (1988 Jan) Vol. 157, No. 1, pp. 149-55.
Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States.
Language: English.

We molecularly cloned the gag and env genes of the human immunodeficiency AB virus (HIV) and expressed fragments of these genes in Escherichia coli. Using the recombinant core and envelope proteins, we developed two competitive immunoassays (CIAs). Samples that recognized either the envelope or core proteins were considered positive for antibodies to HIV. This test system was comparable with western blot in detecting antibodies in patients with AIDS or AIDS-related complex that were repeatably reactive in the HIV screening test. All 360 individuals who were positive by western blot were positive by the CIA. A total of 844 samples repeatably reactive by an ELISA screening test were negative both by western blot and by the CIA; 48 samples positive by ELISA, but negative or indeterminate by western blot, were positive by the CIA. Alternate research procedures verified the positivity of these individuals. These data indicate that the CIA described here may be useful as an adjunct or alternative to the western blot.

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                E SCHEFFEL JAMES W/IN
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E KONRATH J G/IN

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L38 ANSWER 1 OF 5
                       MEDLINE on STN
     Immunohistochemical assessment of estrogen and progesterone receptors in
     stored imprints and cryostat sections of breast carcinomas.
L38 ANSWER 2 OF 5
                       MEDLINE on STN
     Absence of estrogen receptor in human melanoma as evaluated by a
     monoclonal antiestrogen receptor antibody.
L38 ANSWER 3 OF 5
                       MEDLINE on STN
     Detection of estrophilin in frozen sections of breast cancers using an
     estrogen receptor immunocytochemical assay.
L38 ANSWER 4 OF 5
                       MEDLINE on STN
     Use of a monoclonal anti-estrogen receptor antibody in the
     immunohistochemical evaluation of human tumors.
L38 ANSWER 5 OF 5
                      MEDLINE on STN
     Estrogen receptor analyses. Correlation of biochemical and
     immunohistochemical methods using monoclonal antireceptor antibodies.
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                   QUI WEI/AU
F.2
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E3
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                   QUI X H/AU
E6
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                   QUI X J/AU
E7
             1
                   QUI X K/AU
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E9
              1
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E10
              4
                    OUI Y/AU
E11
              2
                    QUI Y H/AU
E12
              2
                    QUI Y L/AU
=> s e3
L39
              3 "QUI X"/AU
=> d 139,ti,1-3
L39 ANSWER 1 OF 3
                       MEDLINE on STN
     Comparison of high-resolution structures of the diphtheria toxin repressor
     in complex with cobalt and zinc at the cation-anion binding site.
L39 ANSWER 2 OF 3
                       MEDLINE on STN
     Cloning and characterization of PO22, a pollen-expressed gene in alfalfa.
L39 ANSWER 3 OF 3
                       MEDLINE on STN
     Chinese medical school exit objectives: a multi-institutional survey of
     teacher opinion.
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E2
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E3
F.4
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E7
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E8
             2
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L7
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L21
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        718603 ANTIBOD?
L42
            10 L41 AND ANTIBOD?
=> d 142,ti,1-10
L42 ANSWER 1 OF 10
                        MEDLINE on STN
     Monoclonal antibodies to an HIV-1 group O envelope recombinant.
L42 ANSWER 2 OF 10
                        MEDLINE on STN
     Significance of the anti-E2 response in self-limited and chronic hepatitis
     C virus infections in chimpanzees and in humans.
L42 ANSWER 3 OF 10
                        MEDLINE on STN
     A search for hepatitis C virus polymerase chain reaction-positive but
     seronegative subjects among blood donors with elevated alanine
     aminotransferase.
L42 ANSWER 4 OF 10
                       MEDLINE on STN
     RETROCELL HIV-1 passive hemagglutination assay for HIV-1 antibody
     screening.
L42 ANSWER 5 OF 10
                        MEDLINE on STN
     {\tt AMLR-reactive}\ {\tt T}\ {\tt cells}\ {\tt isolated}\ {\tt by}\ {\tt autologous}\ {\tt rosette}\ {\tt formation}.
L42 ANSWER 6 OF 10
                        MEDLINE on STN
     Inhibition of autologous rosette formation by monoclonal antibody to the
     sheep erythrocyte receptor.
L42 ANSWER 7 OF 10
                        MEDLINE on STN
     Immune response to immobilized sheep erythrocyte monolayer.
L42 ANSWER 8 OF 10
                        MEDLINE on STN
     Induction of polyclonal immunoglobulin synthesis in porcine peripheral
     blood lymphocytes by pokeweek mitogen.
L42 ANSWER 9 OF 10
                        MEDLINE on STN
     Age dependency of spontaneous anti-autologous erythrocyte plaque-forming
     cells among cultured rabbit appendix cells.
L42 ANSWER 10 OF 10
                         MEDLINE on STN
     Spontaneous plaque-forming cells against autologous erythrocytes develop
     in cultures of normal rabbit appendix cells.
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                E HUNT JEFFREY C/IN
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L3
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L26

3 S L25 AND ANTIBOD?

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L5
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L7
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L8
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L9
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                E HUNT J C/IN
L14
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L15
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L16
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                E KONRATH J G/IN
1.18
              8 S E3
L19
              0 S L18 NOT (L12 OR L14)
                E QIU X/IN
L20
             357 S E3 ·
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             15 S L20 AND ANTIBOD?
L22
              8 S L21 AND (HIV)
L23
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L24
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L25
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              3 S L25 AND ANTIBOD?
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L27
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L29
L30
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L33
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L34
             10 S L33 AND HIV
L35
              9 S L34 NOT L31
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L36
              6 S E2-E3
L37
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L38
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L39
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L40
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L41
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L42
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=> e tyner j d/au
E1
             6
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E2
             1
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E3
             1 --> TYNER J D/AU
E4
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             8
E5
             3
                   TYNER J J/AU
E6
                   TYNER J JEFFREY/AU
             1
F.7
             1
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E8
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E.9
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E10
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E11
                   TYNER K D/AU
             1
E12
             2
                   TYNER KATHERINE M/AU
=> s e3
Ĺ43
             1 "TYNER J D"/AU
=> e tyner joan d/au
E.1
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E2
             8
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E3
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             2
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E7
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E12
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=> d 143,ti
L43 ANSWER 1 OF 1
                       MEDITNE on STN
     Probing ligand protein binding equilibria with fluorescence fluctuation
     spectroscopy.
=> file uspatful
COST IN U.S. DOLLARS
                                                  SINCE FILE
                                                                   TOTAL
                                                       ENTRY
                                                                SESSION
FULL ESTIMATED COST
                                                        7.61
                                                                 167.09
FILE 'USPATFULL' ENTERED AT 08:10:10 ON 24 JUL 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 20 Jul 2006 (20060720/PD)
FILE LAST UPDATED: 20 Jul 2006 (20060720/ED)
HIGHEST GRANTED PATENT NUMBER: US7080410
HIGHEST APPLICATION PUBLICATION NUMBER: US2006162035
CA INDEXING IS CURRENT THROUGH 20 Jul 2006 (20060720/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 20 Jul 2006 (20060720/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006
=> s (HIV or human immunodeficiency virus)
         44285 HIV
        511460 HUMAN
         25087 IMMUNODEFICIENCY
        103169 VIRUS
         17874 HUMAN IMMUNODEFICIENCY VIRUS
                 (HUMAN (W) IMMUNODEFICIENCY (W) VIRUS)
         46622 (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L44
=> s 144 and (antibody capture)
        120497 ANTIBODY
        166470 CAPTURE
          1063 ANTIBODY CAPTURE
                 (ANTIBODY(W)CAPTURE)
L45
           403 L44 AND (ANTIBODY CAPTURE)
=> s 145 and (capsid or p24 or p26)
          9240 CAPSID
          6151 P24
          1899 P26
L46
            71 L45 AND (CAPSID OR P24 OR P26)
=> s 145 and capture/clm
         23235 CAPTURE/CLM
L47
            39 L45 AND CAPTURE/CLM
=> s 147 and ay<2001
       3216819 AY<2001
L48
            14 L47 AND AY<2001
=> d 148,ti,1-14
L48 ANSWER 1 OF 14 USPATFULL on STN
ΤI
       PCR ASSAY
    ANSWER 2 OF 14 USPATFULL on STN
TI
       Hybrid one-step immunochromatographic device and method of use
L48 ANSWER 3 OF 14 USPATFULL on STN
ΨT
      Method for performing Rubella assay
L48
   ANSWER 4 OF 14 USPATFULL on STN
       Therapeutic and diagnostic methods using total leukocyte surface
       antigens
L48 ANSWER 5 OF 14 USPATFULL on STN
       Up-converting reporters for biological and other assays using laser
       excitation techniques
L48 ANSWER 6 OF 14 USPATFULL on STN
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amplification

- L48 ANSWER 7 OF 14 USPATFULL on STN
- TI Immunoassay diagnostic kit
- L48 ANSWER 8 OF 14 USPATFULL on STN
- TI Detection of an analyte by fluorescence using a thin film optical device
- L48 ANSWER 9 OF 14 USPATFULL on STN
- TI Ion-capture assays using a specific binding member conjugated to carboxymethylamylose
- L48 ANSWER 10 OF 14 USPATFULL on STN
- TI Methods and reagents for performing ion-capture digoxin assays
- L48 ANSWER 11 OF 14 USPATFULL on STN
- TI Methods for using CKS fusion proteins
- L48 ANSWER 12 OF 14 USPATFULL on STN
- TI , Monoclonal antibodies to specific antigenic regions of the **human** immunodeficiency virus and methods for use
- L48 ANSWER 13 OF 14 USPATFULL on STN
- TI Method of detecting antigenic, nucleic acid-containing macromolecular entities
- L48 ANSWER 14 OF 14 USPATFULL on STN
- TI Time-resolved fluorescence immunoassay
- => d 148,cbib,clm,12,7
- L48 ANSWER 12 OF 14 USPATFULL on STN
- 92:29607 Monoclonal antibodies to specific antigenic regions of the human

immunodeficiency virus and methods for use.

Flesher, Alan R., Seattle, WA, United States Shriver, Mary K., Bellevue, WA, United States

Genetic Systems Corporation, Redmond, WA, United States (U.S. corporation) US 5104790 19920414

APPLICATION: US 1987-105761 19871007 (7)

DOCUMENT TYPE: Utility; Granted.

- CAS INDEXING IS AVAILABLE FOR THIS PATENT.
- CLM What is claimed is:
  - 1. A method for detecting and/or quantitating HIV in a biological sample suspected of containing HIV or antigenic determinants of HIV, said method comprising: a) incubating the sample with capture monoclonal antibodies obtained from HB 9407 and/or HB 9408, and, either simultaneously or sequentially, with a labelled antibody composition binding to antigenic determinants of HIV, such that specific binding occurs, thereby forming a reaction mixture; and b) detecting the reaction mixture formed in step (a) to determine the amount of label associated with the antigenic determinants and thereby detecting and/or quantitating HIV or antigenic determinants of HIV present in the sample.
  - 2. The method of claim 1, wherein the labeled antibody composition is one or more monoclonal antibodies.
  - 3. The method of claim 2, wherein the monoclonal antibody is obtained from cell line  ${\tt HB}$  9408 or  ${\tt HB}$  9409.
  - 4. The method of claim 1, wherein the labeled antibody composition is a polyclonal antiserum.
  - 5. The method of claim 4, wherein the polyclonal antibodies are obtained from a human previously exposed to **HIV** and containing antibodies to said virus.
  - 6. The method of claim 1, wherein the **capture** monoclonal antibodies are immobilized on a solid phase.
  - 7. The method of claim 1, wherein the label is selected from the group consisting of radionuclides, fluorescers, enzymes, enzyme substrates, enzyme cofactors, enzyme inhibitors, and ligands.
  - 8. The method of claim 1, wherein the sample is selected from the group consisting of bodily secretions, bodily fluids, tissue specimens, cultured cells, and cell culture supernatants.
  - 9. The method of claim 1, wherein the step of detection is by enzyme reaction, fluorescence, radioactivity, cell lysis, or luminescent emission.

comprising compartments containing in a first compartment a monoclonal antibody obtained from cell line ATCC No. HB 9407 or HB 9408 and a second compartment containing a second monoclonal antibody obtained from ATCC No. HB 9409 and labels providing for a detectable signal covalently bonded to said second monoclonal antibody or bonded to antibodies specifically reactive with said second monoclonal antibody.

- 11. The cell line ATCC No. HB 9407, HB 9408 or HB 9409.
- 12. A monoclonal antibody produced by a cell line of claim 11.

L48 ANSWER 7 OF 14 USPATFULL on STN 97:31567 Immunoassay diagnostic kit.

Gould, Martin, Gibbstown, NJ, United States Vulimiri, Sudhakar, West Deptford, NJ, United States Ampcor, Inc., Bridgeport, NJ, United States (U.S. corporation) US 5620845 19970415

APPLICATION: US 1994-306250 19940914 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. An immunoassay process for the detection of a target immunologically active agent in a liquid sample comprising: a) contacting said liquid sample containing said target immunologically active agent to be assayed with a labeled capture reagent against said target immunologically active agent, and with a controlled effective amount of a bound capture reagent against said target immunologically active agent bound to a solid carrier member over only a portion thereof in a controlled substantially specific array and wherein the remaining portion of said solid carrier member having been treated with animal serum and with a solution of a casein protein in an effective amount is substantially blocked against bonding to said labeled capture reagent and said target immunologically active agent; and b) detecting the presence of said target immunologically active agent by determining the label bound to said bound capture reagent on said solid carrier member as an indication of the presence of the target immunologically active agent in said fluid sample.
- 2. The immunoassay process according to claim 1, wherein the presence of target immunologically active agent is detected without washing the solid carrier member.
- 3. The process according to claim 2, wherein said target immunologically active agent is an antigen.
- 4. The process according to claim 3, wherein said labeled capture reagent is an enzyme labeled antibody against said target antiqen.
- 5. The immunoassay process according to claim 3, wherein said solid carrier member is a film of non-fibrous material and said bound capture reagent is applied to and bound over only a portion of one surface of said solid carrier member by jet-type atomizer means in a controlled narrow linear band containing a controlled amount of said bound capture reagent.
- 6. The immunoassay process according to claim 5, wherein said solid carrier member is a polymeric material to which said bound **capture** reagent is bound.
- 7. The immunoassay process according to claim 6, wherein said bound capture reagent consists essentially of an immobilized antibody against said target immunologically active agent and said labeled capture reagent is an antibody reagent against said target immunologically active agent to which is attached a label.
- 8. The process according to claim 2, wherein said labeled **capture** reagent and said bound **capture** reagent are monoclonal or polyclonal antibodies or mixtures thereof.
- 9. The process according to claim 2, wherein said liquid sample is a body fluid, culture media, food or water.
- 10. The process according to claim 1, wherein said labeled **capture** reagent is an enzyme labeled antibody and the determining label step comprises contacting said solid carrier member with a color forming solution selected to generate a color change of the enzyme label which is visual.
- 11. The process according to claim 10, wherein said color forming solution is in a time-release form in an admixture of said fluid sample of target immunologically active agent and said labeled **capture** reagent.

- 12. An immunoassay process for the detection of a target immunologically active agent in a liquid sample consisting essentially of admixing said liquid sample containing said target immunologically active agent with a labeled **capture** reagent against said target immunologically reactive agent, contacting said admixture with a controlled effective amount of a bound capture reagent against said target immunologically active agent, said bound capture reagent being applied to and bound to a solid carrier member by jet-type atomizer means over only one surface thereof in a controlled substantially specific array and wherein the remaining portion of said solid carrier member is substantially blocked against bonding to said labeled capture reagent and said target immunologically reactive agent, and then contacting said bound capture reagent without washing the same with a color forming solution selected for detecting the presence of the target immunologically active agent by determining by visualization an indication of the presence of label bound to said bound capture reagent on said carrier member.
- 13. The immunoassay process according to claim 12, wherein said target immunologically active agent is an antigen.
- 14. The immunoassay process according to claim 13, wherein said solid carrier member is a polymeric material to which said bound **capture** reagent is bound and wherein the remaining portion of said solid carrier member is treated with animal serum and with a solution of a casein protein in an effective amount to substantially block the same.
- 15. The immunoassay process according to claim 14, wherein said bound **capture** reagent consists essentially of an immobilized antibody reagent against said target immunologically active agent and said labeled **capture** reagent is an antibody reagent against said target immunologically active agent to which is attached a label.
- 16. The immunoassay process according to claim 15, wherein said solid carrier member is a thin film of non-fibrous polymeric material to which said bound **capture** reagent is bound in a controlled linear or dot-like pattern consisting essentially of a controlled effective amount of said bound **capture** reagent.
- 17. The immunoassay process according to claim 16, wherein said bound **capture** reagent is chemically and/or absorptively bound to said carrier member.
- 18. The immunoassay process according to claim 16, wherein said labeled antibody reagent is an enzyme labeled antibody reagent.
- 19. The immunoassay process according to claim 13, wherein said antigen is selected from the group consisting of chorigonadotropin, Salmonella, Epstein-Barr, Chlamydia, an antigen of Lyme disease, Escherichia coli, Proteus, Kiebsiella, Staphylococcus, Pseudomonas and Hepatitis A & B.
- 20. The immunoassay process according to claim 12, wherein said solid carrier member is removed from contact with said reaction admixture and is directly placed in contact with said color-forming solution in a separate container without washing.

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(FILE 'HOME' ENTERED AT 07:45:40 ON 24 JUL 2006)

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L2
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             18 S E3
L3
L4
             10 S L3 NOT L1
1.5
             10 S L4 AND ANTIBOD?
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              8 S E3
L6
L7
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                E OUI XIAOXING/IN
                E SCHEFFEL JAMES W/IN
1.8
              9 S E3
1.9
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                E TYNER JOAN D/IN
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1.10
L11
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                 E HUNT J C/IN
              15 S E3
L14
L15
              14 S L14 AND ANTIBOD?
             12 S L15 AND (HIV)
L16
L17
               4 S L16 NOT L12
                 E KONRATH J G/IN
T.18
               8 S E3
L19
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                E QIU X/IN
             357 S E3
L20
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L22
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L24
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L25
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              3 S L25 AND ANTIBOD?
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L36
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L37
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L38
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                E QUI X/AU
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L39
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L40
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L41
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T.44
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L45
1.46
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L47
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L48
             14 S L47 AND AY<2001
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         37250 ANTIBODY/CLM
         23235 CAPTURE/CLM
            19 ANTIBODY CAPTURE/CLM
                 ((ANTIBODY(W)CAPTURE)/CLM)
L49
             2 L45 AND (ANTIBODY CAPTURE/CLM)
=> d 149, ti, 1-2
L49 ANSWER 1 OF 2 USPATFULL on STN
TI
       c-myc coding region determinant-binding protein (CRD-BP) and its nucleic
       acid sequence
L49
    ANSWER 2 OF 2 USPATFULL on STN
       Up-converting reporters for biological and other assays using laser
       excitation techniques
=> s 144 and (antibody/clm and antigen/clm)
         37250 ANTIBODY/CLM
         17194 ANTIGEN/CLM
L50
          3050 L44 AND (ANTIBODY/CLM AND ANTIGEN/CLM)
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           661 CAPSID/CLM
           231 P24/CLM
            57 P26/CLM
L51
           100 L50 AND (CAPSID/CLM OR P24/CLM OR P26/CLM)
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L13

=> s 151 and ay<2001 3216819 AY<2001

L52 41 L51 AND AY<2001

=> d 152, ti, 1-10

L52 ANSWER 1 OF 41 USPATFULL on STN TI AAV4 VECTOR AND USES THEREOF

L52 ANSWER 2 OF 41 USPATFULL on STN

TI Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

L52 ANSWER 3 OF 41 USPATFULL on STN

Method for simultaneous detection of HIV antigens and HIV antibodies

L52 ANSWER 4 OF 41 USPATFULL on STN

TI Use of heat shock proteins

L52 ANSWER 5 OF 41 USPATFULL on STN

TI FUSION PROTEINS BETWEEN ANTIGENIC AMINO ACID SEQUENCES AND BETA-2-MICROGLOBULIN

L52 ANSWER 6 OF 41 USPATFULL on STN

Monoclonal antibodies to human immunodeficiency virus and uses thereof

L52 ANSWER 7 OF 41 USPATFULL on STN

TI Process for detecting Borna disease virus (BDV) infections

L52 ANSWER 8 OF 41 USPATFULL on STN

TI METHODS FOR THE DETECTION OF HTLV-II ANTIBODIES EMPLOYIING NOVEL HTLV-II nra ENVELOPE PEPTIDES

L52 ANSWER 9 OF 41 USPATFULL on STN

TI Kits for the detection of human immunodeficiency virus type 2 (HIV-2) antigens

L52 ANSWER 10 OF 41 USPATFULL on STN

TI Methods for producing members of specific binding pairs

=> d 152,cbib

L52 ANSWER 1 OF 41 USPATFULL on STN
2003:305990 AAV4 VECTOR AND USES THEREOF.

CHIORINI, JOHN A., SILVER SPRINGS, MD, UNITED STATES KOTIN, ROBERT M., BETHESDA, MD, UNITED STATES SAFER, BRIAN, SILVER SPRINGS, MD, UNITED STATES US 2003215422 Al 20031120

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WO 1997-US16266 19970911

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 152,cbib,6

L52 ANSWER 6 OF 41 USPATFULL on STN

2002:198536 Monoclonal antibodies to **human immunodeficiency virus** and uses thereof.

Lou, Sheng C., Libertyville, IL, UNITED STATES Hunt, Jeffrey C., Mundelein, IL, UNITED STATES Konrath, John G., Lake Villa, IL, UNITED STATES Qiu, Xiaoxing, Gurnee, IL, UNITED STATES Scheffel, James W., Mundelein, IL, UNITED STATES Tyner, Joan D., Beach Park, IL, UNITED STATES US 2002106636 A1 20020808

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DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 152,cbib,clm,1-41

L52 ANSWER 1 OF 41 USPATFULL ON STN
2003:305990 AAV4 VECTOR AND USES THEREOF.
CHIORINI, JOHN A., SILVER SPRINGS, MD, UNITED STATES
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SAFER, BRIAN, SILVER SPRINGS, MD, UNITED STATES
US 2003215422 A1 20031120
APPLICATION: US 1999-254747 A1 19991126 (9)

PRIORITY: US 1996-60025934 19960911 DOCUMENT TYPE: Utility; APPLICATION. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A nucleic acid vector comprising a pair of adeno-associated virus 4 (AAV4) inverted terminal repeats and a promoter between the inverted terminal repeats.
- 2. A nucleic acid vector comprising a pair of adeno-associated virus 4 (AAV4) inverted terminal repeats and a promoter between the inverted terminal repeats, wherein the AAV4 inverted terminal repeats comprise the nucleotide sequence set forth in SEQ ID NO:6.
- 3. A nucleic acid vector comprising a pair of adeno-associated virus 4 (AAV4) inverted terminal repeats and a promoter between the inverted terminal repeats, wherein the AAV4 inverted terminal repeats comprise the nucleotide sequence set forth in SEQ ID NO:20.
- 4. The vector of claim 2, wherein the promoter is an AAV promoter p5.
- 5. The vector of claim 4, wherein the p5 promoter is AAV4 p5 promoter.
- 6. The vector of claim 2, further comprising an exogenous nucleic acid functionally linked to the promoter.
- $7.\ \mbox{The vector of claim 2 encapsidated in an adeno-associated virus particle.}$
- 8. The particle of claim 7, wherein the particle is an AAV4 particle, comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4.
- 9. The particle of claim 7, wherein the particle is an AAV1 particle, an AAV2 particle, an AAV3 particle or an AAV5 particle.
- 10. An AAV4 particle, comprising a capsid protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4.
- 11. The particle of claim 10, wherein the vector further comprises an exogenous nucleic acid inserted between the inverted terminal repeats.
- 12. An isolated nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:1.
- 13. An isolated nucleic acid consisting essentially of the nucleotide sequence set forth in SEQ ID NO:1.
- 14. An isolated nucleic acid that selectively hybridizes with the nucleic acid of claim 13.
- 15. An isolated nucleic acid encoding an adeno-associated virus 4 Rep protein.
- 16. The nucleic acid of claim 15, wherein the adeno-associated virus 4 Rep protein has the amino acid sequence set forth in SEQ D No:2.
- 17. The nucleic acid of claim 15, wherein the adeno-associated virus 4 Rep protein has the amino acid sequence set forth in SEQ ID NO:8.
- 18. The nucleic acid of claim 15, wherein the adeno-associated virus 4 Rep protein has the amino acid sequence set forth in SEQ ID NO:9.
- 19. The nucleic acid of claim 15, wherein the adeno-associated virus 4 Rep protein has the amino acid sequence set forth in SEQ ID NO:10.
- 20. The nucleic acid of claim 15, wherein the adeno-associated virus 4 Rep protein has the amino acid sequence set forth in SEQ ID NO:11.
- 21. The nucleic acid of claim 15, wherein the nucleic acid comprises the nucleotide sequence set forth in  $SEQ\ ID\ No:3$ .
- 22. The nucleic acid of claim 15, wherein the nucleic acid consists essentially of the nucleotide sequence set forth in SEQ ID NO:3.
- 23. An isolated nucleic acid that selectively hybridizes with the nucleic acid of claim 22.
- 24. The nucleic acid of claim 15, wherein the nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO:12.
- 25. The nucleic acid of claim 15, wherein the nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO:13.

- 26. The nucleic acid of claim 15, wherein the nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO:14.
- 27. The nucleic acid of claim 15, wherein the nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO:15.
- 28. An isolated AAV4 Rep protein having the amino acid sequence set forth in SEQ ID NO:2, or a unique fragment thereof.
- $29.\ \mbox{An isolated AAV4}$  Rep protein having the amino acid sequence set forth in SEQ ID NO:8, or a unique fragment thereof.
- 30. An isolated AAV4 Rep protein having the amino acid sequence set forth in SEQ ID NO:9, or a unique fragment thereof.
- 31. An isolated AAV4 Rep protein having the amino acid sequence set forth in SEQ ID NO:10, or a unique fragment thereof.
- 32. An isolated AAV4 Rep protein having the amino acid sequence set forth in SEQ ID NO:11, or a unique fragment thereof.
- 33. An isolated  ${\bf antibody}$  that specifically binds the protein of claim 28.
- 34. An isolated AAV4  ${f capsid}$  protein having the amino acid sequence set forth in SEQ ID NO:4.
- 35. An isolated antibody that specifically binds the protein of claim 34.
- 36. An isolated AAV4  ${f capsid}$  protein having the amino acid sequence set forth in SEQ ID NO:16.
- 37. An isolated **antibody** that specifically binds the protein of claim 36.
- 38. An isolated AAV4  ${f capsid}$  protein having, the amino acid sequence set forth in SEQ ID NO:18.
- 39. An isolated  ${\bf antibody}$  that specifically binds the protein of claim 38.
- 40. An isolated nucleic acid encoding the adeno-associated virus 4 capsid protein of SEQ ID NO:16.
- 41. An isolated nucleic acid encoding the adeno-associated virus 4 capsid protein of SEQ ID No:4.
- 42. The nucleic acid of claim 41, wherein the nucleic acid comprises the nucleic acid sequence set forth in SEQ D No:5.
- 43. The nucleic acid of claim 41, wherein the nucleic acid consists essentially of the nucleic acid sequence set forth in SEQ ID NO:5.
- 44. An isolated nucleic acid that selectively hybridizes with the nucleic acid of claim 39.
- 45. An isolated nucleic acid that selectively hybridizes with the nucleic acid of SEQ ID NO:4.
- 46. An isolated nucleic acid comprising the AAV4 p5 promoter comprising nucleotides 130-291 of SEQ ID NO:1.
- 47. A method of screening a cell for infectivity by AAV4 comprising contacting the cell with an AAV4 particle comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4 and detecting the presence of the AAV4 particle in the cells.
- 48. A method of screening a cell for infectivity by AAV4 comprising contacting the cell with an AAV4 vector comprising an AAV4 particle comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4 and comprising a known nucleic acid, wherein the presence of the AAV4 vector is detected in the cells by detecting the presence of the known nucleic acid.
- 49. A method of determining the suitability of an AAV4 vector for administration to a subject comprising administering to an antibody-containing sample from the subject an antigenic protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:2, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11 and residues 438-601of SEQ ID NO:2

presence of a reaction indicating the AAV4 vector to be unsuitable for use in the subject.

- 50. A method of determining the presence in a subject of an AAV4-specific **antibody** comprising administering to an **antibody**-containing sample from the subject an antigenic protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:2, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11 and residues 438-601 SEQ ID NO:4 and detecting an **antibody-antigen** reaction in the sample, the presence of a reaction-indicating the presence of an AAV4-specific **antibody** in the subject.
- 51. A method of delivering a nucleic acid to a cell comprising administering to the cell an AAV4 particle, comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4, containing a vector comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats, thereby delivering the nucleic acid to the cell.
- 52. The method of claim 52, wherein the AAV inverted terminal repeats are AAV4 inverted terminal repeats.
- 53. The method of claim 52, wherein the AAV inverted terminal repeats are AAV2 inverted terminal repeats.
- 54. A method of delivering a nucleic acid to a subject comprising administering to a cell from the subject an AAV4 particle, comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4, comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats, and returning the cell to the subject, thereby delivering the nucleic acid to the subject.
- 55. A method of delivering a nucleic acid to a cell in a subject comprising administering to the subject an AAV4 particle, comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4, comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats, thereby delivering the nucleic acid to a cell in the subject.
- 56. A method of delivering a nucleic acid to a cell in a subject having antibodies to AAV2 comprising administering to the subject an AAV4 particle, comprising a **capsid** protein comprising an amino acid sequence defined by amino acids 438-601 shown in SEQ ID NO:4, comprising the nucleic acid, thereby delivering the nucleic acid to a cell in the subject.
- 57. The vector of claim 3, wherein the promoter is an AAV promoter p5.
- 58. The vector of claim 3, wherein the p5 promoter is AAV4 p5 promoter.
- $59.\ \,$  The vector of claim 3, further comprising an exogenous nucleic acid functionally linked to the promoter.
- $60.\ \mbox{The vector}$  of claim 3, encapsidated in an adeno-associated virus particle.
- 61. The particle of claim 61, wherein the particle is an AAV4 particle, comprising a  ${f capsid}$  protein comprising an amino acid sequence defined by amino acids 43 8-601 shown in SEQ ID NO:4.
- 62. The particle of claim 61, wherein the particle is an AAV1 particle, an AAV2 particle, an AAV3 particle or an AAV5 particle.
- 63. An isolated nucleic acid encoding, the adeno-associated virus 4 capsid protein of SEQ ID NO:18.
- 64. The particle of claim 7, wherein the particle is an AAV4 particle, comprising a **capsid** protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16 and SEQ ID NO:18.
- 65. An AAV4 particle, comprising a **capsid** protein consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16 and SEQ ID NO:18, containing a vector comprising a pair of AAV2 inverted terminal repeats.
- 66. A method of delivering a nucleic acid to a cell comprising administering to the cell an AAV4 particle, comprising a **capsid** protein consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16 and SEQ ID NO:18, containing a vector comprising the nucleic acid inserted between a pair of AAV-inverted terminal repeats, thereby delivering the nucleic acid to

- 67. A method of delivering a nucleic acid to a subject comprising administering to a cell from the subject an AAV4 particle, comprising a capsid protein consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16 and SEQ ID NO:18, comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats, and returning the cell to the subject, thereby delivering the nucleic acid to the subject.
- 68. A method of delivering a nucleic acid to a cell in a subject comprising administering to the subject an AAV4 particle, comprising a **capsid** protein consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16 and SEQ ID NO:18, comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats, thereby delivering the nucleic acid to a cell in the subject.
- 69. A method of delivering a nucleic acid to a cell in a subject having antibodies to AAV2 comprising administering to the subject an AAV4 particle, comprising a **capsid** protein consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:16 and SEQ ID NO:18, comprising the nucleic acid, thereby delivering the nucleic acid to a cell in the subject.
- 70. An AAV4 vector, comprising a nucleic acid selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22.
- 71. An isolated adeno-associated virus 4 Rep protein.

L52 ANSWER 2 OF 41 USPATFULL on STN
2003:210083 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination.
Stemmer, Willem P. C., Los Gatos, CA, United States
Crameri, Andreas, Mountain View, CA, United States
Maxygen, Inc., Redwood City, CA, United States (U.S. corporation)
US 6602986 B1 20030805

APPLICATION: US 2000-713920 20001115 (9)

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. An **antibody** comprising a heavy chain comprising three nonnaturally occuring CDR regions, and a light chain comprising three nonnaturally occurring CDR regions, wherein the **antibody** specifically binds to a human **antigen**.
- 2. An **antibody** comprising a heavy chain comprising three nonnaturally occurring CDR regions, and a light chain comprising three nonnaturally occurring CDR regions, wherein the six nonnaturally occurring CDRs are the CDRs of SEQ. ID. Nos. 28-33 respectively.
- 3. The antibody of claim 1 that binds to a human antigen selected from the group consisting of CD4, CD8, IL-2 receptor, EGF receptor and PDGF receptor.
- 4. An **antibody** comprising a heavy chain comprising three nonnaturally occurring CDR regions, and a light chain comprising three nonnaturally occurring CDR regions, wherein the **antibody** specifically binds to human thrombomodulin, protein C, carbohydrate **antigen**, sialyl Lewis **antigen**, or electin.
- 5. An **antibody** comprising a heavy chain comprising three nonnaturally occurring CDR regions, and a light chain comprising three nonnaturally occurring CDR regions, wherein the **antibody** specifically binds to an **antigen** selected from the group consisting of bacterial LPS, virion **capsid** protein and envelope glycoprotein.
- 6. An **antibody** comprising a heavy chain comprising three nonnaturally occurring CDR regions, and a light chain comprising three nonnaturally occurring CDR regions, wherein the heavy and light chains are linked as a single chain via a linker peptide.
- 7. An **antibody** comprising a heavy chain comprising three nonnaturally occurring CDR regions, and a light chain comprising three nonnaturally occurring CDR regions, wherein the **antibody** specifically binds with an affinity of at least  $10^8 \text{ M}^{-1}$ .

Donie, Frederic, Penzberg, GERMANY, FEDERAL REPUBLIC OF Faatz, Elke, Huglfing, GERMANY, FEDERAL REPUBLIC OF Upmeier, Barbara, Iffeldorf, GERMANY, FEDERAL REPUBLIC OF Hoess, Eva, Munich, GERMANY, FEDERAL REPUBLIC OF Buyse, Marie-Ange, Melsen, BELGIUM Saman, Eric, Bornem, BELGIUM Roche Diagnostics GmbH, Mannheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation) US 6593079 B1 20030715 WO 9840744 19980917 APPLICATION: US 2000-381009 20000112 (9) WO 1998-EP1235 19980305 PRIORITY: DE 1997-19709762 19970310 DE 1997-19727943 19970701 DOCUMENT TYPE: Utility; GRANTED. CAS INDEXING IS AVAILABLE FOR THIS PATENT. What is claimed is:

CLM

- 1. An immunoassay method for the detection of at least one of antibodies and antigens of each of HIV1, HIV1-sub0 and HIV2 in a sample suspected of containing said antibodies and antigens, the method comprising: a) incubating binding partners R1 and R2 in a sample mixture comprising at least a portion of said sample, wherein R1 binds specifically to an antigen selected from the group consisting of the p24 antigen of HIV1, the p24 antigen of HIV1-Sub0 and the p26 antigen of HIV2, R1 being bound directly or indirectly to a first solid phase, and wherein R2 binds specifically to said antigen, R2 being bound to a first detectable label, and R2 recognizing an epitope different from that recognized by R1, whereby the antigen forms a sandwich with R1
- and R2; b) incubating binding partners R3 and R4 in a sample mixture comprising at least a portion of said sample, wherein R3 binds specifically to a first  $\mbox{antibody}$  selected from the group consisting of antibodies against an antigen of the env region HIV1, HIV1-Sub0 and HIV2, R3 being bound directly or indirectly to a second solid phase, and wherein R4 binds specifically to the first antibody, R4 being bound to a second detectable label, whereby said first antibody forms a bridge between R3 and R4; c) incubating binding partners R5 and R6 in a sample mixture comprising at least a portion of said sample, wherein R5 binds specifically to a second antibody selected from the group consisting of antibodies against an antigen of the pol and gag regions of HIV1. HIV-Sub0 and HIV2, wherein the gag regions exclude sequences of p24 and p26, R5 being bound directly or indirectly to a third solid phase, and wherein R6 binds specifically to the second antibody, R6 being bound to a third detectable label, whereby the second antibody forms a bridge between R5 and R6; and d) determining the amount of the detectable labels bound to the solid phases or remaining unbound as a measure of the antibodies and the antigens of HIV1, HIV1-sub0, and HIV2 in the sample; wherein at least one of R1, R3, and R5 binds specifically to at least one of antibodies and antigens of HIV1; at least one of R1, R3, and R5 binds specifically to at least one of antibodies and antigens
- 2. The method of claim 1, wherein R1 is an antibody produced from a cell line selected from the group consisting of cell lines mAb<p24>M-6A9/5, deposit number DSM ACC2310, mAb<p24>M-4B1/1, deposit number DSM ACC2299, mAbp24>M-6D9/4, deposit number DSM ACC2300 or mAb<p24>M-2E7/3, deposit number DSM ACC2301.

at least one of antibodies and antigens of HIV2.

of HIV-SubO; and at least one of R1, R3, and R5 binds specifically to

- 3. The method of claim 1, wherein R1 is an antibody against an HIV1 p24 antigen, the antibody binding in an equivalent way to an antibody produced from a cell line selected from the group consisting of cell lines mAb<p24>M-6A9/5, deposit number DSM ACC2310, mAb<p24>M-4B1/1, deposit number DSM ACC2299, mAb<p24>M-6D9/4, deposit number DSM ACC2300 or mAb<p24>M-2E7/3, deposit number DSM ACC2301.
- 4. The method of claim 1, wherein R1 is an antibody against an HIV1 p24 antigen, the antibody binding to the same epitope as an antibody produced from a cell line selected from the group consisting of cell lines mAb<p24>M-6A9/5, deposit number DSM ACC2310, mAb<p24>M-4B1/1, deposit number DSM ACC2299, mAb<p24>M-6D9/4, deposit number DSM ACC2300 or mAb<p24>M-2E7/3, deposit number DSM ACC2301.
- 5. The method of claim 1, wherein the incubating binding partners R1 and R2 and the incubating binding partners R3 and R4 are performed simultaneously in the same sample mixture.
- 6. The method of claim 1, wherein the incubating binding partners R3 and  $\ensuremath{\mathsf{R4}}$  and the incubating binding partners  $\ensuremath{\mathsf{R5}}$  and  $\ensuremath{\mathsf{R6}}$  are performed simultaneously in the same sample mixture.

R2 and the incubating binding partners R5 and R6 are performed simultaneously in the same sample mixture.

- 8. The method of claim 1, wherein the incubating binding partners R1 and R2, the incubating binding partners R3 and R4, and the incubating binding partners R5 and R6 are performed simultaneously in the same sample mixture.
- 9. The method of claim 1, wherein the sample is selected from a group consisting of whole blood, blood sera, blood plasma, urine, and saliva.
- 10. A reagent kit for detection of an HIV infection, said kit comprising: binding partners R1, R2, R3, R4, R5, and R6; wherein R1 binds specifically to an antigen selected from the group consisting of the p24 antigen of HIV1, the p24 antigen of HIV1-Sub0 and the p26 antigen of HIV2, R1 being bound directly or indirectly to a solid phase; R2 binds specifically to said antigen, R2 being bound to a detectable label, and R2 recognizing an epitope different from that recognized by R1, whereby said antigen forms a sandwich with R1 and R2; R3 binds specifically to a first **antibody** selected from the group consisting of antibodies against an antigen of the env region of HIVI, HIV1-Sub0 and HIV2, R3 being bound directly or indirectly to a solid phase; R4 binds specifically to said first antibody, R4 being bound to a detectable label, whereby said first antibody forms a bridge between R3 and R4; R5 binds specifically to a second antibody selected from the group consisting of antibodies against an antigen of the pol and gag regions of HIV1, HIV1-Sub-0 and HIV2, wherein said gag regions exclude sequences of p24 and p26, R5 being bound directly or indirectly to a solid phase; R6 binds specifically to said second antibody, R6 being bound to a detectable label, whereby said second antibody forms a bridge between R5 and R6; and wherein at least one of R1, R3, and R5 binds specifically to at least one of antibodies and antigens of HIV1; at least one of R1, R3, and R5 binds specifically to at least one of antibodies and antigens of HIV-Sub0; and at least one of R1, R3, and R5 binds specifically to at least one of antibodies and antigens of HIV2.
- 11. The reagent kit of claim 10, wherein R1 comprises an **antibody** produced from a cell line selected from the group consisting of cell lines mAb<**p24**>M-6A9/5, deposit number DSM ACC2310, mAb<**p24**>M-4B1/1, deposit number DSM ACC2299, mAb<**p24**>M-6D9/4, deposit number DSM ACC2300 or mAb<**p24**>M-2E7/3, deposit number DSM ACC2301.
- 12. The reagent kit of claim 10, wherein R2 comprises an **antibody** produced from a cell line selected from the group consisting of cell lines mAb< $\mathbf{p24}$ >M-6A9/5, deposit number DSM ACC2310, mAb< $\mathbf{p24}$ >M-4B1/1, deposit number DSM ACC2299, mAb< $\mathbf{p24}$ >M-6D9/4, deposit number DSM ACC2300 or mAb< $\mathbf{p24}$ >M-2E7/3, deposit number DSM ACC2301.

L52 ANSWER 4 OF 41 USPATFULL on STN
2003:187409 Use of heat shock proteins.
Lehner, Thomas, London, UNITED KINGDOM
Kelly, Charles George, London, UNITED KINGDOM
Wang, Yufei, London, UNITED KINGDOM
US 2003129195 Al 20030710

APPLICATION: US 2002-168901 A1 20020923 (10) WO 2000-GB4957 20001221

PRIORITY: GB 1999-30443 19991222 DOCUMENT TYPE: Utility: APPLICATION. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. Use of a heat shock protein to enhance production of one or more chemokines and/or a suppressor factor by a cell.
- 2. The use of claim 1, wherein the one or more chemokines is at least one of RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ .
- 3. The use of claim 1 or claim 2, wherein the heat shock protein is HSP27, HSP40, HSP60, HSP65, HSP70 or HSP96.
- 4. The use of any one of the previous claims, wherein the heat shock protein is  ${\tt HSP70}$ .
- 5. The use of any one of the previous claims, wherein the heat shock protein does not comprise a heterologous peptide.
- 6. The use of any one of the previous claims, wherein the heat shock protein does not comprise an heterologous immunogenic peptide.
- 7. The use of any one of claims 1 to 4, wherein one or more peptides are linked to the heat shock protein.

- 9. The use of claim 8, wherein at least one of the one or more peptide is gp120 or  $\mathbf{p24}$  from  $\mathbf{HIV}$ .
- 10. The use of claim 7 or claim 8, wherein at least one of the one or more peptides is derived from the extracellular domains of CCR5.
- 11. The use of claim 8, wherein at least one of the one or more peptides comprises the sequence MDYQVSSPIYDINYYTSEPC; HYAAAQWDFGNTMCQ; CSSHFPYSQYQFWKNFQTLK, DINYYTSEPCQKINVKQIAAR, RSQKEGLHYTCSSHFPYSQY or NTFQEFFGLNNCSSSNRLDQ.
- 12. The use of any one of claims 7 to 11, wherein at least one of the one or more peptides is covalently linked to the heat shock protein.
- 13. The use of claim 12, wherein at least one of the one or more peptides is covalently linked to the heat shock protein via a linker.
- 14. The use of claim 13, wherein the linker is glutaraldehyde.
- 15. The use of claim 13, wherein the linker is N-succinimydyl-3(2-pyridyldithio)propionate.
- 16. The use of any one of claims 7 to 11 wherein at least one of the one or more peptides is non-covalently linked to the heat shock protein.
- 17. The use of claim 12, wherein at least one of the one or more peptides has a hydrophobic region capable of non-covalently binding to the heat shock protein.
- 18. The use of a heat shock protein which does not comprise a heterologous immunogenic peptide in the manufacture of a composition for the treatment or prophylaxis of an infectious disease.
- 19. The use of claim 18, wherein the infectious disease is an  ${f HIV}$  infection.
- 20. The use of claim 18 or claim 19, wherein the heat shock protein is HSP27, HSP40, HSP65, HSP60, HSP96 or HSP70.
- $22.\$ The use of any one of claims 18 to 21, wherein the heat shock protein does not comprise a heterologous peptide.
- 23. The use of any one of claims 18 to 21, wherein one or more non-immunogenic peptides are linked to the heat shock protein.
- 24. The use of claim 23, wherein at least one of the one or more non-immunogenic peptides is covalently linked to the heat shock protein.
- 25. The use of claim 24, wherein at least one of the one or more non-immunogenic peptides is covalently linked to the heat shock protein via a linker.
- 26. The use of claim 24, wherein the linker is glutaraldehyde.
- 27. The use of claim 24, wherein the linker is N-succinimy dyl-3(2-pyridyldithio) propionate.
- 28. The use of claim 23 wherein at least one of the one or more peptides is non-covalently linked to the heat shock protein.
- 29. The use of claim 28, wherein at least one of the one or more peptides has a hydrophobic region capable of non-covalently binding to the heat shock protein.
- 30. A method of treatment or prophylaxis of an infectious disease, comprising administering to a patient in need of such treatment or prophylaxis an effective dose of a heat shock protein which does not comprise a heterologous immunogenic protein.
- 31. A heat shock protein linked to one or more immunogenic peptides of CCR5 or one or more immunogenically similar peptides for the treatement or prophylaxis of an infectious disease.
- 32. The heat shock protein of claim 31, wherein at least one of the one or more immunogenic peptides comprises the sequence MDYQVSSPIYDINYYTSEPC, HYAAAQWDFGNTMCQ, CSSHFPYSQYQFWKNFQTLK,

one or more immunogenically similar peptides.

- 33. The heat shock protein of claim 31 or claim 32, wherein at least one of the one or more peptides is covalently linked to the heat shock protein.
- 34. The heat shock protein of claim 33, wherein at least one of the one or more peptides is covalently linked to the heat shock protein via a linker.
- $35.\$ The heat shock protein of claim  $33,\$ wherein the linker is glutaraldehyde.
- 36. The heat shock protein of claim 33, wherein the linker is N-succinimydyl-3(2-pyridyldithio)propionate.
- 37. The heat shock protein of claim 31 or claim 32 wherein at least one of the one or more peptides is non-covalently linked to the heat shock protein.
- 38. The heat shock protein of claim 37, wherein at least one of the one or more peptides has a hydrophobic region capable of non-covalently binding to the heat shock protein.
- 39. A pharmaceutical composition comprising a heat shock protein according to any one of claims 31 to 38 in combination with a pharmaceutically acceptable excepient, carrier, adjuvant or vehicle.
- 40. The heat shock protein according to any one of claims 31 to 38 for use in therapy.
- 41. Use of a heat shock protein according to any one of claims 31 to 38 in the manufacture of a medicament for the treatement or prophylaxis of an infectious disease.
- 42. A method of treatment or prophylaxis of an infections disease, comprising administering to a patient in need of such treatment or prophylaxis an effective dose of a heat shock protein according to any one of claims 31 to 38.
- 43. The use of claim 41 or the method of claim 42, wherein the infectious disease is an  ${f HIV}$  infection.
- 44. A peptide from an extracellular domain of CCR5 or an immunogenically similar peptide for use as an  ${f antigen}$ .
- 45. The peptide of claim 44, wherein the peptide comprises the sequence MDYQVSSPIYDINYYTSEPC, HYAAAQWDFGNTMCQ, CSSHFPYSQYQFWKNFQTLK, DNYTSEPCQKINVQIAAR, RSQKEGLHYTCSSHFPYSQY or NTFQEFFGLNNCSSSNRLDQ.
- 46. The peptide of claim 44, wherein the peptide has the sequence MDYQVSSPIYDINYYTSEPC, HYAAAQWDFGNTMCQ, CSSHFPYSQYQFWKNFQTLK, DINYYTSEPCQKINVKQIAAR, RSQKEGLHYTCSSHFPYSQY or NTFQEFFGLNNCSSSNRLDQ.
- 47. A pharmaceutical composition comprising a peptide according to any one of claims 44 to 46 in combination with a pharmaceutically acceptable excepient, carrier, adjuvant or vehicle.
- 48. The peptide of any one of claims 44 to 46 or the pharmaceutical composition of claim 47 for use in therapy.
- 49. Use of the peptide of any one of claims 44 to 46 as an **antigen** to generate antibodies having affinity for CCR5.
- 50. An  ${\it antibody}$  molecule having affinity for the peptide of any one of claims 44 to 46.
- 51. A pharmaceutical composition comprising the peptide of any one of claims 44 to 46 or the **antibody** molecule of claim 50 in combination with a pharmaceutically acceptable excepient, carrier, adjuvant or vehicle.
  - 52. Use of the peptide of any one of claims 44 to 46 or the **antibody** molecule of claim 50 in the manufacture of a medicament for the treatment or prophylaxis of an **HIV** infection.
  - 53. A method of treatment or prophylaxis of an infectious disease, comprising administering to a patient in need of such treatment or prophylaxis an effective dose of the peptide of any one of claims 44 to 46 or the **antibody** molecule of claim 50.
  - 54. The use of a heat shock protein to release chemokines and thereby

infection of malignant disease.

- 55. The use according to claim 45, in which the heat shock protein is linked to a peptide.
- 56. The use according to claim 46, in which the peptide is derived from the extracellular domains of CCR5.
- 57. The use of a heat shock protein optionally linked to a smaller peptide in the manufacture of a medicament for the treatment or prevention of a microbial infection or a malignant disease.
- 58. A method of increasing the inflammatory response to microbial (including virus) infections or malignant disease which comprises administering a heat shock protein to a subject suffering therefrom or susceptible thereto.
- 59. A pharmaceutical composition containing a heat shock protein for parenteral administration in accordance with the method defined in claim 49.
- 60. A use, method, or composition as defined in any of claims 1 to 6, in which the heat shock protein is selected from HSP65, HSP60, HSP96, HSP70, HSP40 and HSP27.
- 61. A use, method, or composition according to claim 50, in which the heat shock protein is HSP70 or HSP65.
- 62. A use, method, or composition according to any of the preceding claims, in which the heat shock protein is linked to a carrier material e.g. a peptide.
- 63. A use, method, or composition according to any of the preceding claims, in which the heat shock protein is administered subcutaneously, intramuscularly, or mucosally in amounts of from about 50 to about 500 micrograms per unit dose.
- L52 ANSWER 5 OF 41 USPATFULL on STN

2002:227955 FUSION PROTEINS BETWEEN ANTIGENIC AMINO ACID SEQUENCES AND BETA-2-MICROGLOBULIN.

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APPLICATION: US 1995-532549 A1 19951201 (8) WO 1994-GB755 19940408

PRIORITY: GB 1993-7311 19930408 DOCUMENT TYPE: Utility: APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A hybrid fusion protein comprising a first antigenic amino acid sequence fused directly or indirectly to the N-terminus of a second amino acid sequence substantially homologous to beta-2-microglobulin (B2M) or a fragment thereof, characterised in that the first antigenic amino acid sequence corresponds to a sequence derived from or associated with a tumour or an aetiological agent, other than E.coli OmpA signal sequence.
- 2. A fusion protein as claimed in claim 1 where the second amino acid sequence is that of naturally occurring B2  $\rm M_{\odot}$
- 3. A fusion protein as claimed in claim 1 where the aetiological agent is a microorganism such as a virus, bacterium, fungus or parasite.
- 4. A fusion protein as claimed in claim 3 where the virus is a retrovirus, such as HIV-1, HIV-2, HTLV-I, HTLV-II, HTLV-III, SIV, BIV, LAV, ELAV, CIAV, murine leukaemia virus, Moloney murine leukaemia virus, and feline leukaemia virus; an orthomyxovirus, such as influenza A or B; a paramyxovirus, such as parainfluenza virus, mumps, measles, RSV and Sendai virus; a papovavirus, such as HPV; an arenavirus, such as LCMV of humans or mice; a hepadnavirus, such as Hepatitis B virus; a herpes virus, such as HSV, VZV, CMV, or EBV.
- 5. A fusion protein as claimed in claim 3 where the antigenic sequence is derived from a bacterium, such as of the genus Neisseria, Campylobacter, Bordetella, Listeria, Mycobacteria or Leishmania, or a parasite, such as from the genus Trypanosoma, Schizosoma, Plasmodium, especially P. falciparum, or from a fungus, such as from the genus Candida, Aspergillus, Cryptococcus, Histoplasma or Blastomyces.
- 6. A fusion protein as claimed in claim 1 where the antigenic sequence is a proteinaceous human tumour antigen, such as a melanoma-associated

breast or colon carcinoma.

7. A fusion protein as claimed in claim 3 where the antigenic sequence is an epitope from: 1) HIV (particularly HIV-1) gp120, 2) HIV (particularly HIV-1) p24 3) VZV gpI, gpII and gpIII 4) LCMV nucleoprotein, 5) Influenza virus nucleoprotein, 6) HPV L1 and L2 proteins, 7) Human papilloma virus E5 and E7 8) Malaria CSP or RESA antigens, 9) Mycobacterium p6, 10) GA 733-2 epithelial tumour-associated antigen, 11) MUC-1 repeat sequence from epithelial tumour-associated antigen, 12) Melanoma MZ2-E antigens 13) Melanoma p97 associated antigen,

- 8. A fusion protein as claimed in claim 3 where the antigenic sequence is an epitope from the third variable domain of an envelope protein of a lentivirus.
- 9. A fusion protein as claimed in any of the preceding claims wherein the antigenic sequence is fused to the B2 M via a linker sequence.
- 10. Nucleic acid coding for a fusion protein as claimed in any one of claims 1 to 9.
- 11. A vector including nucleic acid as claimed in claim 10.
- 12. A host cell carrying a vector as claimed in claim 11.
- 13. A host cell as claimed in claim 12 where the host cell is E. coli
- 14. A host cell as claimed in claim 12 where the host cell is a yeast cell such as Saccharomyces cerevisiae or Pichia pastoris
- 15. Host cells as claimed in claim 12 where the host cell is an insect cell such as Spodoptera frugiperda SF9, or mammalian cells including Chinese hamster ovary (CHO) cells, mouse myeloma cell lines such as P3X63-Ag8.653, COS cells, HeLa cells, BHK cells, melanoma cell lines such as the Bowes cell line, mouse L cells, human hepatoma cell lines such as Hep G2, mouse fibroblasts and mouse NIH 3T3 cells.
- 16. A pharmaceutical or veterinary formulation comprising a B2 M fusion protein as claimed in any one of claims 1-9 and a pharmaceutically or veterinarily acceptable carrier.
- 17. A pharmaceutical or veterinary formulation as claimed in claim 16 comprising in addition a subunit vaccines designed to induce good neutralising **antibody** responses.
- 18. A B2 M fusion protein as claimed in any one of claims 1-9 for use as a prophylactic or immunotherapeutic vaccine.
- 19. The use of a B2 M fusion protein as claimed in any one of claims 1-9 in the preparation of a prophylactic or immunotherapeutic vaccine
- 20. A method of producing a B2 M fusion protein as claimed in any of claims 1-9 by cultivating a methylotropic yeast harbouring an expression vector comprising DNA encoding the relevant fusion protein, and recovering the expressed fusion protein.
- 21. A method as claimed in claim 20 where the yeast is Pichia pastoris.
- L52 ANSWER 6 OF 41 USPATFULL on STN

2002:198536 Monoclonal antibodies to **human immunodeficiency virus** and uses thereof.

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APPLICATION: US 2000-731126 A1 20001206 (9)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- A monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26.
- 2. The monoclonal **antibody** of claim 1 wherein said **antibody** is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.

binds to a shared epitope **Human Immunodeficiency Virus**-1 protein **p24** and **Human Immunodeficiency Virus**-2 protein **p26**.

4. The hy	ybridoma cel	l line of	f claim 3,	wherein sa:	id cell 1	ine is	
selected	from the gr	oup consi	isting of A	A.T.C.C. Dep	oosit No.	нв	
A.T.C.C.	Deposit No.	HB	, A.T.C	.C. Deposit	No. HB		
A.T.C.C.	Deposit No.			.C. Deposit			and
A.T.C.C.	Deposit No.	нв		•	_		

- 5. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and b) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.
- 6. The method of claim 5 wherein said at least one monoclonal **antibody** of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 7. The method of claim 6 wherein said at least one monoclonal **antibody** of step (a) is labeled.
- 8. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Ruman Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; b) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and c) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.
- 9. The method of claim 8 wherein said at least one monoclonal antibody of step (a) is selected from the group consisting of 120A-270, 115B-151 117-289, 103-350, 115B-303, and 108-394.
- 10. The method of claim 8 wherein said **antibody** of step (b) of said conjugate is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303, and 108-394.
- 11. The method of claim 8 wherein said at least one monoclonal **antibody** of step (a) is selected from the group consisting of 120-270, 108-394 and 115B-303, and said **antibody** of step (b) of said conjugate is selected from the group consisting of 117-289 and 115B-151.
- 12. The method of claim 11 wherein said at least one monoclonal **antibody** of step (a) is 120A-270 and said **antibody** of step (b) of said conjugate is 115B-151.
- 13. A method for detecting the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV antigen, in a test sample suspected of containing one or more of said antigens, comprising the steps of: (a) contacting: 1) at least one monoclonal antibody which binds to a shared epitope of HIV-1 p24 antigen and HIV-2 p26 antigen bound to a solid support, 2) said test sample, and 3) an indicator reagent comprising an antibody which binds to HIV-1 antigen and HIV-2 antigen to which a signal generating compound is attached, to form a mixture; (b) incubating said mixture for a time and under conditions sufficient to form antibody/antigen/antibody complexes; (c) detecting presence of a measurable signal generating by said signal-generating compound, presence of said signal indicating presence of one or more antigens in said test sample selected from the group consisting of HIV-1 antigen and HIV-2 antigen.
- 14. The method of claim 13 wherein said at least one monoclonal **antibody** of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.

- 15. The method of claim 13 wherein said **antibody** of said indicator reagent of step (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 16. The method of claim 13 wherein said at least one monoclonal antibody of step (a) is 120A-270 and said antibody of said indicator reagent of of step (a) is 115B-151.
- 17. A kit for determining the presence of one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26; and (b) a conjugate comprising an antibody attached to a signal generating compound capable of generating a detectable signal.
- 18. The kit of claim 17 wherein said at least one monoclonal **antibody** of (a) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.
- 19. The kit of claim 17 wherein said antibody of (b) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-3-3 and 108-394.
- 20. A diagnostic reagent comprising at least one monoclonal **antibody** selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 108-394 and 115B-303.
- 21. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:1.}$
- 22. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:2.}$
- 23. An isolated peptide comprising the amino acid sequence of SEQ ID  $\ensuremath{\mathsf{N0:3.}}$
- $24.\ \mbox{An}$  isolated peptide comprising the amino acid sequence of SEQ ID  $\mbox{NO:}\,4.$
- 25. An isolated peptide comprising the amino acid sequence of SEQ ID  ${\tt NO:5.}$
- 26. An isolated peptide comprising the amino acid sequence of SEQ ID  $\ensuremath{\mathsf{NO:6}}.$
- 27. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of  ${f HIV}-1$ antigen/HIV-1 antibody complexes; b) detecting said HIV-1 antigen/HIV-1 antibody complexes, presence of said complexes indicating presence of **HIV-1** antibody in said test sample; c) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes; d) detecting said HIV-2 antigen/HIV-2 antibody complexes, presence of said complexes indicating presence of HIV-2 antibody in said test sample; e) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and f) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.
- 28. A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of: a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes: b) adding a conjugate to the resulting HIV-1 antigen/HIV-1 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound

www.g.g. mileteti buta oonjuguee oompttood un mempus uleugiju ee u signal generating compound capable of generating a detectable signal; c) detecting HIV-1 antibody which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of HIV-1 antibody in said test sample; d) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes: e) adding a conjugate to the resulting HIV-2 antigen/HIV-2 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal; f) detecting HIV-2 antibody which may be present in said test sample by detecting a signal generated by said signal-generating compound, presence of said signal indicating presence of HIV-2 antibody in said test sample; g) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; h) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and i) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.

L52 ANSWER 7 OF 41 USPATFULL on STN

2002:136749 Process for detecting Borna disease virus (BDV) infections.

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APPLICATION: US 2000-582615 20000629 (9)
WO 1998-DE3793 19981224 20001128 PCT 371 date

PRIORITY: DE 1997-19758017 19971229 DOCUMENT TYPE: Utility; GRANTED.

- 1. A process for detecting Borna disease virus (BDV) infection in an animal, comprising (a) contacting a body fluid specimen with a first antibody specific for a circulating immune complex (CIC) indicative of BDV infection, which immune complex comprises a BDV antigen and an antibody to BDV antigen, and (b) detecting binding between said first antibody and said immune complex, wherein said binding is indicative of infection.
- 2. A process according to claim 1, additionally comprising detecting the presence of at least one BDV **antigen** in said body fluid specimen, by using a second **antibody** originating from a species different from said first **antibody**, wherein said second **antibody** is BDV-specific.
- 3. A process according to claim 2, wherein said BDV antigen is BDV nucleoprotein p40 or BDV-phosphoprotein p24.
- 4. A process according to claim 1, additionally comprising detecting the presence of at least one BDV **antibody** in said body fluid specimen, by binding a standardized solution of native BDV antigens, prepared from infected tissue culture or from brain of infected animals, to said first **antibody**, wherein said at least one BDV **antibody** is indicative of BDV infection and can be detected in said body fluid specimen.
- 5. A process according to claim 2, additionally comprising detecting the presence of at least one BDV **antibody** in said body fluid specimen, by binding a standardized solution of native BDV antigens, prepared from infected tissue culture or from brain of infected animals, to said first **antibody**, wherein said at least one BDV **antibody** is indicative of BDV infection and can be detected in said body fluid specimen.
- 6. A process according to claim 1, wherein said body fluid specimen is a blood, urine or spinal fluid specimen.
- $7.\$ A process according to claim 2, wherein the body fluid specimen is a blood plasma, urine or spinal fluid specimen.
- 8. A process according to claim 2, wherein the body fluid specimen is a blood specimen, and wherein the **antigen** detection is carried out on a leukocyte fraction or on a blood plasma fraction of said blood specimen.

- $9.\ \mbox{A}$  process according to claim 7, wherein all tests are carried out on a blood plasma specimen.
- 10. A process for detecting a BVD circulating immune complex (CIC) of an antigen and an antibody which circulates in a body fluid, comprising: (1) contacting a specimen of said body fluid with a support, wherein said support has monoclonal or polyclonal antibodies that bind to an antigen in said CIC, said monoclonal or polyclonal antibodies being fixed to said support via the Fc region wherein said monoclonal antibodies are monoclonal BDV-specific antibodies that are directed against native BDV antigens, and wherein said native BDV antigens are derived from natural sources; (2) contacting said specimen from (1) with a secondary antibody of a species other than the assayed species, wherein said secondary antibody is specific for antibodies of the species whose body fluid specimen was used; and (3) detecting binding of said secondary antibody to said support.
- 11. A process according to claim 10, wherein the BDV-specific antibodies are selected from the group consisting of N protein-specific antibodies and P protein-specific antibodies.
- 12. A process according to claim 10, wherein the support is an adsorptively fixing polymer assay plate, which is first occupied as completely as possible with secondary antibodies which are specific for the species from which the immune complex-antigen-specific antibodies were obtained, and subsequently the immune complex-antigen-specific antibodies are applied to this layer of secondary antibodies.
- 13. A process according to claim 10, wherein detection of the secondary  ${f antibody}$  in accordance with (3) of the process is done via an EIA or RIA process.
- 14. A process according to claim 13, wherein the secondary **antibody** is coupled to alkaline phosphatase and is visualized with p-nitrophenyl phosphate by means of a color reaction or made selectable by means of optical detectors.
- 15. A diagnostic kit for detecting BDV infection, comprising at least one BDV-specific monoclonal or polyclonal **antibody**, means for contacting these antibodies with a specimen suspected of containing BDV antigens or BDV immune complexes, and means for detecting the attached antigens or immune complexes.
- 16. A diagnostic kit for detecting BDV infection, comprising at least one BDV-specific monoclonal or polyclonal **antibody** occupied by a BDV **antigen**, means for contacting the **antigen**-occupied antibodies with a specimen suspected of containing BDV antibodies, and means for detecting the attached antibodies.
- 17. A diagnostic kit according to claim 15, comprising a unit on or in which the BDV-specific antibodies are present in immobilized form.
- 18. A diagnostic kit according to claim 17, wherein the BDV-specific antibodies are monoclonal or polyclonal antibodies obtained from a first species which are immobilized on a support coated with a species II-anti-species I IgG obtained from a second, different species.
- 19. A diagnostic kit according to claim 18, wherein the support is a solid plate or an assay tube.
- 20. A diagnostic kit according to claim 18, wherein the antibodies from the first species are polyclonal or monoclonal mouse antibodies.
- 21. A diagnostic kit according to claim 20, wherein the antibodies from the first species are selected from the group consisting of P-protein and N-protein specific monoclonal mouse antibodies, and the adsorptive coating of the support is composed of an anti-mouse IgG.
- 22. A diagnostic kit according to claim 21, wherein the anti-mouse  ${\rm Ig}G$  is a goat-anti-mouse  ${\rm Ig}G$ .
- 23. A diagnostic kit according to claim 18, wherein the BDV-specific antibodies are immobilized via polystyrene-bound Clq.
- 24. The process of claim 1, wherein said animal is human.
- 25. The process of claim 24, wherein said human is suffering from a neurological condition.
- 26. The process of claim 25, wherein said neurological condition is selected from the group consisting of depression, and obsessive-compulsive disorder.

L52 ANSWER 8 OF 41 USPATFULL ON STN
2002:78391 METHODS FOR THE DETECTION OF HTLV-II ANTIBODIES EMPLOYIING NOVEL
HTLV-II nra ENVELOPE PEPTIDES.

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APPLICATION: US 1994-259451 A1 19940620 (8) DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. An isolated HTLV-II virus, the genome of said virus comprising the sequence set forth in SEQ ID NO: 1.
- 2. A purified HTLV-II NRA viral lysate.
- 3. The lysate of claim 2 comprising virus from cells deposited as ATCC No. CRL 11580.
- 4. A tissue culture grown cell infected with HTLV-II NRA.
- 5. A HTLV-II virus gag gene expression product.
- 6. The expression product of claim 5 comprising gag protein, p19.
- 7. The expression product of claim 5 comprising gag protein, p24.
- 8. The expression product of claim 5 comprising gag protein, p15.
- 9. A HTLV-II virus pol gene expression product.
- 10. A HTLV-II virus env gene expression product.
- 11. The expression product of claim 10 comprising env protein, p21e. product.
- 12. A HTLV-II virus tax gene expression product.
- 13. A HTLV-II virus rex gene expression product.
- 14. A fusion protein comprising a HTLV-II virus gene expression product, said expression product coded by one of a env, gag, pol, tax or rex gene.
- 15. A method for detecting anti-HTLV-II antibody in a test sample, comprising the following steps: a) providing (i) a test sample suspected of containing anti-HTLV-II antibody, (ii) HTLV-II antigen, said antigen comprising a composition selected from the group consisting of HTLV-II NRA viral lysates, HTLV-II NRA peptides, HTLV-II NRA proteins, and combinations thereof, and (iii) an indicator reagent comprising a detectable label and a binding member specific for said antigen or antibody; b) forming a reaction mixture by contacting the test sample with said antigen and indicator reagent; c) incubating the reaction mixture under conditions sufficient to form antigen/antibody/indicator reagent complexes; and d) detecting the labeled complexes as an indication of the presence of anti-HTLV-II antibody in said test sample.
- 16. The method of claim 15 wherein said HTLV-II antigen is attached to a solid phase.
- 17. The method of claim 16 wherein said solid phase is selected from the group consisting of beads, microparticles and microtiter plate wells.
- 18. The method of claim 15 wherein said detectable label is selected from the group consisting of enzymes, radioisotopes, chemiluminescent and fluorescent labels.

comprises anti-human IgG antibody.

- 20. A method for detecting anti-HTLV-II antibody in a test sample, comprising the following steps: a) providing (i) a test sample suspected of containing anti-HTLV-II antibody, (ii) HTLV-II antigen, said antigen comprising a composition selected from the group consisting of HTLV-II NRA viral lysates, HTLV-II NRA peptides, HTLV-II NRA proteins, and combinations thereof, (iii) an indicator reagent comprising a detectable label and a binding member specific for said antigen or antibody; b) forming a reaction mixture by contacting the test sample with said antigen; c) incubating the reaction mixture under conditions sufficient to form antigen/antibody complexes; d) after incubating, determining the presence or amount of anti-HTLV-II antibody by (i) contacting the reaction mixture with the indicator reagent; (ii) incubating the reaction mixture and the indicator reagent under conditions sufficient to form antigen/antibody/indicator reagent complexes; and (iii) detecting the labeled complexes or the unreacted indicator reagent as an indication of the presence of anti-HTLV-II antibody in said test sample.
- 21. The method of claim 20 wherein said  $\mbox{HTLV-II}$  antigen is attached to a solid phase.
- 22. The method of claim 20 wherein said solid phase is selected from the group consisting of beads, microparticles and microtiter wells.
- 23. The method of claim 20 wherein said detectable label is selected from the group consisting of enzymes, radioisotopes, chemiluminescent and fluorescent labels.
- 24. A method for detecting **antibody** to HTLV-I and/or HTLV-II in a test sample, comprising: (a) providing a test sample suspected of containing HTLV-I antibody and/or HTLV-II antibody; (b) contacting said test sample with HTLV-I antigen and HTLV-II antigen for a time and under conditions sufficient to form antigen/antibody complexes, said HTLV-I antigen comprising a composition selected from the group consisting of HTLV-I viral lysates, HTLV-I peptides, HTLV-I proteins, and combinations thereof, and said HTLV-II antigen comprising a composition selected from the group consisting of HTLV-II NRA viral lysates, HTLV-II NRA peptides, HTLV-II NRA proteins and combinations thereof; (c) contacting said complexes with indicator reagent comprising a detectable label and a binding member specific for said antigens or said antibodies under conditions sufficient to form antigen/antibody/indicator reagent complexes; and (d) detecting the labeled complexes as an indication of anti-HTLV-II antibody, anti-HTLV-II antibody, or both, in said test sample.
- 25. The method of claim 24 wherein said  ${\tt HTLV-II}$  antigen and  ${\tt HTLV-II}$  antigen are attached to a solid phase.
- 26. The method of claim 25 wherein said HTLV-I antigen and HTLV-II antigen are attached to a single solid phase.
- 27. The method of claim 24 wherein said detectable label is selected from the group consisting of enzymes, radioisotopes, chemiluminescent and fluorescent labels.
- 28. The method of claim 24 wherein said indicator reagent binding member comprises an anti-human IgG **antibody**.
- $29.\ \mbox{The method of claim 24 wherein steps (b)}$  and (c) are performed simultaneously.
- 30. The method of claim 25 wherein said HTLV-II antigen and HTLV-II antigen are attached to separate solid phases.
- 31. The method of claim 30 wherein said indicator reagent binding member comprises  $\mbox{HTLV-I}$  antigen and  $\mbox{HTLV-II}$  antigen.
- 32. The method of claim 31 wherein said indicator reagent detectable label comprises biotin.
- 33. An article of manufacture, comprising: a container; a label on said container; and a composition contained within said container; wherein the composition is effective for detecting anti-HTLV-II antibody, the label on said container indicates that the composition can be used for detecting anti-HTLV-II antibody, and the effective agent in said composition comprises HTLV-II antigen selected from the group consisting of HTLV-II NRA viral lysates, HTLV-II NRA peptides, HTLV-II NRA proteins and combinations thereof.
- 34. The article of manufacture of claim 33 wherein said label on said

composition.

35. A kit, comprising: a first container, a label on said container, and a composition contained within said container; wherein the composition is effective for detecting anti-HTLV-II antibody, the label on said container indicates that the composition can be used for detecting anti-HTLV-II antibody, and the effective agent in said composition comprises HTLV-II antigen selected from the group consisting of HTLV-II NRA viral lysates, HTLV-II NRA peptides, HTLV-II NRA proteins and combinations thereof; and a second container comprising isotonic diluent.

- 36. The kit of claim 35 wherein said HTLV-II antigen is attached to a solid phase.
- 37. The kit of claim 35 further comprising HTLV-I antigen.
- 38. A reagent comprising nonfat dry milk, serum, and buffer, said reagent effective in reducing nonspecific binding.
- L52 ANSWER 9 OF 41 USPATFULL on STN

2001:167701 Kits for the detection of human immunodeficiency virus type 2 (HIV-2) antigens.

Montagnier, Luc, Le Plessis Robinson, France

Guetard, Denise, Paris, France

Brun-Vezinet, Francoise, Paris, France

Clavel, Francois, Paris, France

Institut Pasteur, Paris, France (non-U.S. corporation)

US 6296807 B1 20011002

APPLICATION: US 1998-143095 19980828 (9)

PRIORITY: FR 1986-910 19860122

FR 1986-911 19860122 FR 1986-1635 19860206

FR 1986-1985 19860213

DOCUMENT TYPE: Utility; GRANTED.

CLM What is claimed is:

- 1. A kit for detection an HIV-2 antigen in a biological preparation comprising: (a) a container comprising at least one antibody, which specifically binds to a protein of HIV-2, wherein said protein is selected from the group consisting of gp36, p16, and p26 of HIV-2 MIR or HIV-2 ROD, deposited at the COLLECTION NATIONALE DES CULTURES DE MICRO-ORGANISMES (CNCM) under No. I-502 and No. I-532, respectively; and (b) a container comprising detection means for identifying immunological complexes formed between said antibody and said protein of **HIV-**2.
- 2. The kit of claim 1, wherein said antibody which specifically binds to a protein of HIV-2 is monoclonal.
- 3. The kit of claim 1, wherein said protein of HIV-2 is gp36.
- 4. The kit of claim 2, wherein said protein of HIV-2 is qp36.
- 5. The kit of claim 1, wherein said protein of HIV-2 is gp16.
- 6. The kit of claim 2, wherein said protein of HIV-2 is gpl6.
- 7. The kit of claim 1, wherein said protein of HIV-2 is gp26.
- 8. The kit of claim 2, wherein said protein of HIV-2 is gp26.

## L52 ANSWER 10 OF 41 USPATFULL on STN

2001:63824 Methods for producing members of specific binding pairs.

Winter, Gregory Paul, Cambridge, United Kingdom Johnson, Kevin Stuart, Cambridge, United Kingdom

Griffiths, Andrew David, Cambridge, United Kingdom

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(non-U.S. corporation) Medical Research Council, London, United Kingdom (non-U.S. corporation)

US 6225447 B1 20010501

## APPLICATION: US 1998-98944 19980617 (9)

PRIORITY: GB 1991-10549 19910515

GB 1992-6318 19920324

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

> 1. A specific binding pair member which is a single chain specific binding pair member comprising a first polypeptide chain component and a second polypeptide chain component and specific for a complementary

opeotite binaing pair member or inserteel, produced by a meened mire. comprises: (I) introducing into host cells; (i) first vectors comprising nucleic acid encoding a genetically diverse population of a first polypeptide chain component fused to a component of a secreted replicable genetic display package for display of said polypeptide chain component at the surface of replicable genetic display packages; and (ii) second vectors comprising nucleic acid encoding a genetically diverse population of said second polypeptide chain component; said first vectors being packaged in infectious replicable genetic display packages and their introduction into host cells being by infection into host cells harboring said second vectors; or said second vectors being packaged in infectious replicable genetic display packages and their introducing into host cells being by infection into host cells harboring said first vectors; (II) causing or allowing recombination between said first and second vectors within said host cells, the recombination being promoted by inclusion in said first and second vectors of sequences at which site-specific recombination occurs resulting in recombinant vectors each of which comprises nucleic acid encoding a said single chain specific binding pair member comprising a said first polypeptide chain component and a said second polypeptide chain component and an amino acid sequence encoded by a sequence provided by recombination between said sequences at which site-specific recombination occurs, and capable of being packaged into a replicable genetic display packages using said replicable genetic display package component; (III) expressing said single chain specific binding pair members within the host cells to form a library of said single chain specific binding pair members displayed by replicable genetic display packages, whereby the genetic materials of each said replicable genetic display package encodes a single chain specific binding pair member displayed at its surface, (IV) selecting by binding with said complementary specific binding pair member of interest one or more single chain specific binding pair members specific for said complementary specific binding pair member of interest, each single chain specific binding pair member thus selected being associated in its respective replicable genetic display package with nucleic acid encoding that single chain specific binding pair member, (V) obtaining nucleic acid encoding a said single chain specific binding pair member from its replicable genetic display package displaying a single chain specific binding pair member selected in step (IV); (V) producing, by expression of encoding nucleic acid in a recombinant host organism, a single chain specific binding pair member comprising a first polypeptide chain component and a second polypeptide chain component and an amino acid sequence encoded by a sequence provided by recombination between said sequences at which site-specific recombination occurs and specific for said complementary specific binding pair member of interest, which single chain specific binding pair comprises a polypeptide chain component which is as encoded by nucleic acid encoding a said polypeptide chain component of a specific binding pair member selected in step (IV) or is a derivative thereof by way of addition, deletion, substitution or insertion of one or more amino acids or by linkage of another molecule.

- 2. A specific binding pair member according to claim 1 wherein at least one of said first and second vectors is a phage vector.
- 3. A specific binding pair member according to claim 1 wherein expression in said step (III) is from a phagemid vector, the method including using a helper phage or a plasmid expressing complementing phage genes, to help package said phagemid genome, and said component of the replicable genetic display package is a **capsid** protein therefor.
- 4. A specific binding pair member according to claim 1 wherein either or both of the populations of said first and second polypeptide chain components is derived from a repertoire selected from the group consisting of: (i) the repertoire of rearranged immunoglobulin genes of an animal immunized with a complementary sbp member; (ii) the repertoire of rearranged immunoglobulin genes of an animal not immunized with a complementary sbp member; (iii) a repertoire of an artificially rearranged immunoglobulin gene or genes; (iv) a repertoire of an immunoglobulin homolog gene or genes; (v) a repertoire of sequences derived from a germ-line immunoglobulin gene or genes; (vi) a repertoire of an immunoglobulin gene or genes artificially mutated by the introduction of one or more point mutations; and (vii) a mixture of any of (i), (iii), (iii), (iv), (v) and (vi).
- 5. A specific binding pair member according to claim 1 wherein the replicable genetic display package is a bacteriophage, the host is a bacterium, and said component of the replicable genetic display package is a **capsid** protein for the bacteriophage.
- $6.\ A$  specific binding pair member according to claim 5 wherein the phage is a filamentous phage.
- 7. A specific binding pair member according to claim 6 wherein the phage

class II phages Xf, Pf1 and Pf3.

- 8. A specific binding pair member according to claim 6 wherein the first polypeptide chain components are expressed as fusions with the gene III **capsid** protein of phage fd or its counterpart in another filamentous phage.
- 9. A specific binding pair member according to claim 8 wherein the first polypeptide chain components are each inserted in the N-terminal region of the mature **capsid** protein downstream of a secretory leader peptide.
- 10. A specific binding pair member according to claim 5 wherein the first polypeptide chain components are expressed as fusions with the gene III **capsid** protein of phage fd or its counterpart in another filamentous phage.
- 11. A specific binding pair member according to claim 10 wherein the first polypeptide chain components are each inserted in the N-terminal region of the mature **capsid** protein downstream of a secretory leader peptide.
- 12. A specific binding pair member according to claim 5 wherein the host is  ${\sf E.\ coli.}$
- 13. A specific binding pair member according to claim 1, wherein said sequences at which site-specific recombination occurs are loxP sequences.
- 14. A specific binding pair (sbp) member which is a single chain specific binding pair member specific for a counterpart specific binding pair member of interest, produced by a method which comprises: (i) causing or allowing intracellular recombination between (a) first vectors comprising nucleic acid encoding a population of a fusion of a first polypeptide chain component of a specific binding pair member and a component of a secreted replicable genetic display package and (b) second vectors comprising nucleic acid encoding a population of a second polypeptide chain component of a specific binding pair member, at least one of said populations being genetically diverse, the recombination between the vectors being at sequences at which site-specific recombination occurs and resulting in recombinant vectors each of which comprises nucleic acid encoding a single chain specific binding pair member comprising a said first polypeptide chain component, a said second polypeptide chain component, and an amino acid sequence encoded by a sequence provided by recombination between said sequences at which site-specific recombination occurs, which nucleic acid is capable of being packaged using said replicable genetic display package component; and (ii) expressing said single chain specific binding pair members producing replicable genetic display packages which display at their surface said single chain specific binding pair members and which each comprise nucleic acid encoding a said single chain specific binding pair member (iii) selecting by binding with said counterpart specific binding pair member of interest one or more single chain specific binding pair members specific for said counterpart specific binding pair member of interest, each single chain specific binding pair member thus selected being associated in its respective replicable genetic display package with nucleic acid encoding that single chain specific binding pair member; (iv) obtaining nucleic acid encoding a said single chain specific binding pair member from its replicable genetic display package displaying a specific binding pair member selected in step (v); (v)producing, by expression of encoding nucleic acid in a recombinant host organism, a said single chain specific binding pair member comprising a first polypeptide chain component and a second polypeptide chain component and an amino acid sequence encoded by a sequence provided by recombination between said sequences at which site specific recombination occurs and specific for said complementary specific binding pair member of interest, which single chain specific binding pair comprises a polypeptide chain component which is as encoded by nucleic acid encoding a said polypeptide chain component of a specific binding pair member selected in step (v) or is a derivative thereof by way of addition, deletion, substitution or insertion of one or more amino acids or by linkage of another molecule.
- 15. A specific binding pair member according to claim 14 wherein the sequences at which site-specific recombination occurs are loxP sequences and site-specific recombination is catalysed by Cre-recombinase.
- 16. A specific binding pair member according to claim 14 wherein the first vectors are phages or phagemids and the second vectors are plasmids, or the first vectors are plasmids and the second vectors are phages or phagemids, and the intracellular recombination takes place in a bacterial host which replicates plasmids preferentially over phages or phagemids, or which replicates phages or phagemids preferentially over

- 17. A specific binding pair member according to claim 16 wherein said bacterial host is a PolA strain of E. coli or of another gram-negative bacterium.
- 18. A specific binding pair member according to claim 17 which comprises an antibody antigen-binding domain.
- 19. A specific binding pair member according to claim 14 which comprises a single chain Fv immunoglobulin molecule.

L52 ANSWER 11 OF 41 USPATFULL on STN

2001:25636 Immunoreagents reactive with a conserved epitope of human immunodeficiency virus type I (HIV-1) gp120 and methods of use. Ho, David D., Chapaqua, NY, United States Robinson, James E., New Orleans, LA, United States Cedars-Sinai Medical Center, Los Angeles, CA, United States (U.S. corporation)
US 6190871 B1 20010220

APPLICATION: US 1999-267941 19990311 (9)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A method for determining the efficacy of a monoclonal antibody to neutralize primary isolates of Human Immunodeficiency Virus Type 1, said method comprising the steps of: providing a known concentration of H9 cells in a first receptacle, a second receptacle, a third receptacle, a fourth receptacle, and a fifth receptacle, wherein all five receptacles comprise the same concentration of H9 cells for inoculation; providing a primary HIV-1 isolate; adding fifty percent tissue culture infective doses of the primary HIV-1 isolate to four increasing concentrations of the monoclonal antibody, whereby resulting in four different mixtures of primary HIV-1 isolate and monoclonal antibody, wherein each mixture is contained in a separate container, and wherein the monoclonal antibody is selected from the group consisting of monoclonal antibodies produced by the cell line deposited with the ATCC under Accession No. CRL10758 and monoclonal antibodies produced by the cell line deposited with the ATCC under Accession No. CRL10464; inoculating the H9 cells of four of the five receptacles with the four different mixtures of primary HIV-1 isolate and monoclonal antibody, wherein each receptacle receives a mixture from only one container, whereby resulting in four different cultures; providing one control culture by adding a fifty percent tissue culture infective dose of the primary HIV-1 isolate to the fifth receptacle containing only H9 cells; preparing a supernatant from each of the four cultures and the one control culture, whereby resulting in five supernatants; determining the concentration of p24 antigen in each of the five supernatants, wherein the p24 antigen concentration is used as an indicator of virus infection; and determining the efficacy of the antibody to neutralize HIV infection by comparing the concentration of **p24** antigen in each of the five supernatants.

L52 ANSWER 12 OF 41 USPATFULL on STN

1999:124707 Method of intracellular binding of target molecules.

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Haseltine, William A., Cambridge, MA, United States
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US 5965371 19991012

APPLICATION: US 1995-438190 19950509 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A method for the intracellular binding of a target antigen which comprises: (a) intracellular delivery of a nucleotide sequence containing a promoter operably linked to an antibody gene capable of binding to the target antigen; (b) intracellular expression of the antibody, wherein said antibody is intracellularly expressed as a functional antibody where said function is determined by the ability to bind to the target antigen, and wherein said antibody is selected from the group of antibodies consisting of single chain antibodies, single domain heavy chain and Fab; and (c) intracellular binding of the target antigen by said antibody.
- 2. The method of claim 1, wherein the **antibody** capable of binding to the target **antigen** is a single chain variable fragment.
- 3. The method of claim 1, wherein the **antibody** capable of binding to the target **antigen** is a single domain heavy chain.
- 4. The method of claim 1, wherein the antibody capable of binding to

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- 5. The method of claim 1, wherein the target **antigen** is selected from the group of antigens consisting of intermediate metabolites, sugars, lipids, autacoids, hormones, complex carbohydrates, phospholipids, nucleic acids and proteins.
- 6. The method of claim 1, wherein the target  ${\bf antigen}$  is a hapten, an RNA sequence, a DNA sequence or a protein.
- 7. The method of claim 6, wherein the target antigen is a protein.
- 8. The method of claim 1, wherein the target antigen is a protein whose expression results in malignant cellular transformation.
- 9. The method of claim 8, wherein the target **antigen** results in malignant transformation as a result of overexpression of the protein.
- 10. The method of claim 8, wherein the target  ${\bf antigen}$  is an HTLV-1 protein.
- 11. The method of claim 6, wherein the target antigen is a hapten.
- 13. The method of claim 12, wherein the viral encoded protein is an  ${\bf HIV}$  viral encoded protein.
- 14. The method of claim 12, wherein the **antibody** is an **antibody** capable of binding to the envelope glycoprotein or the **capsid** protein.
- 15. The method of claim 13, wherein the  ${\bf antibody}$  is capable of binding to the envelope glycoprotein.
- 16. The method of claim 15, wherein the target antigen is the envelope qp160.
- 17. The method of claim 1, wherein the target  ${\bf antigen}$  is an  ${\bf HIV}$  provirus.
- 18. The method of claim 15, wherein the target protein is the envelope  $\ensuremath{\mathtt{gp41}}$ .
- 19. The method of claim 6 wherein the target  ${\bf antigen}$  is a TAR element or a RRE sequence.
- 20. The method of claim 1, wherein one uses antibodies to more than one target  ${\bf antigen}$ .
- 21. The method of claim 20, wherein the target antigens are virally encoded protein and the antibodies are to at least two different virally encoded proteins.
- 22. The method of claim 21, wherein the virally encoded proteins are  ${f HIV}$  encoded proteins and the antibodies are to at least one structural protein and at least one regulatory protein.
- 23. The method of claim 22, wherein the structural protein is an envelope glycoprotein and the regulatory protein is either the tat or rev protein.
- 24. The method of claim 23, wherein the envelope glycoprotein is gp160.
- 25. The method of claim 24, which further comprises an  ${\bf antibody}$  to  ${\bf HIV}$  gp41.
- 26. The method of claim 12, wherein the **antibody** is to that portion of the **capsid** protein involved in myristylation.
- 27. The method of claim 13, wherein the antibody is to the tat protein.
- 28. The method of claim 1, wherein the  ${\bf antibody}$  gene further encodes an intracellular localization sequence.
- 29. The method of claim 28, wherein more than one **antibody** to the same target are used, wherein the antibodies have different intracellular localization sequences and target the **antigen** at different intracellular locations.
- 30. The method of claim 29, wherein the target **antigen** is a virally encoded **antigen**.

HIV encoded antigen.

- 32. The method of claim 31, wherein the  ${\tt HIV}$  encoded antigen is an envelope glycoprotein.
- 33. The method of claim 12, wherein the  ${\bf antibody}$  gene further encodes an intracellular localization sequence.
- 34. The method of claim 33, wherein the localization sequence for the structural proteins is cytoplasmic.
- 35. The method of claim 33, wherein the viral protein is selected from the group of viral proteins comprising **HIV** tat, **HIV** rev, HTLV-1 tax, HTLV-1 rex, HTLV-2 tax, and HTLV-2 rex, and the localization sequence is a nuclear localization sequence.
- 36. The method of claim 13, wherein the **antibody** is to that portion of the **capsid** protein involved in myristylation.
- $37.\ \mbox{The method of claim 12, wherein the virally encoded protein is a DNA virus encoded protein.}$
- 39. The method of claim 1, wherein the target antigen is an oncogene.
- 40. The method of claim 1, wherein the target **antigen** is selected from the group consisting of sis, int-2, erbB, neu, fins, ros, kit, abl, src, ras, and erbA.
- 41. The method of claim 1, wherein the cell is an animal or bird cell.
- 42. The method of claim 41, wherein the cell is an animal cell.
- 43. The method of claim 42, wherein the animal is a mammalian cell.
- 44. A method for the intracellular binding of a target antigen, comprising: (a) introducing an antibody cassette into a cell, wherein said antibody cassette contains a nucleic acid segment encoding a light chain of an antibody and a nucleic acid segment encoding a heavy chain of an antibody operably linked to at least one promoter wherein the antibody cassette encodes a single chain antibody or Fab'; (b) intracellular expression of said antibody encoded by said nucleic acid segments encoding said light chain and said heavy chain; and (c) intracellular binding of said target antigen by said antibody.
- 45. The method of claim 44, wherein said nucleic acid segment encoding said light chain is linked to said nucleic acid segment encoding said heavy chain by a nucleic acid segment encoding a linker which is in-frame with nucleic acid segments to produce a single chain **antibody**.
- 46. The method of claim 44, wherein said linker is SEQ ID NO:1.
- 47. The method of claim 44, wherein the **antibody** expressed by the **antibody** cassette is a Fab'.
- 48. The method of claim 44, wherein the target antigen is a protein.
- 49. The method of claim 44, wherein the target **antigen** is a protein whose expression results in malignant cellular transformation.
- 50. The method of claim 49, wherein the target **antigen** results in malignant transformation as a result of overexpression of the protein.
- 51. The method of claim 44, wherein the target antigen is a viral-encoded protein.
- 52. The method of claim 51, wherein the viral encoded protein is an  ${\bf HIV}$  viral-encoded protein.
- 53. The method of claim 52, wherein the target **antigen** is an **HIV** regulatory protein.
- $54.\ \mbox{The method of claim } 53,$  wherein the regulatory protein is the rev protein.
- 55. The method of claim 51, wherein the antibody is an antibody capable of binding to the envelope glycoprotein.
- 56. The method of claim 55, wherein the target antigen is the HIV envelope gp160.

- $57.\ \mbox{The method of claim 44, wherein the target $antigen$ is a TAR element or a RRE sequence.}$
- 58. The method of claim 44, wherein the cell is an animal or bird cell.
- 59. The method of claim 58, wherein the cell is an animal cell.
- 60. The method of claim 59, wherein the animal is a mammalian cell.
- 61. A method for the intracellular binding of a target **antigen**, which comprises: (a) delivery of a nucleic acid segment encoding a single chain **antibody** and a promoter operably linked to said nucleic acid segment to the interior of a cell; (b) intracellular expression of said single chain **antibody**; and (c) intracellular binding of said target **antigen** by said single chain **antibody**.
- 62. The method of claim 61, wherein the target antigen is a protein.
- 63. The method of claim 61, wherein the target **antigen** is a protein whose expression results in malignant cellular transformation.
- 64. The method of claim 63, wherein the target **antigen** results in malignant transformation as a result of overexpression of the protein.
- 65. The method of claim 61, wherein the target **antigen** is a viral-encoded protein.
- 66. The method of claim 65, wherein the viral encoded protein is an  ${\bf HIV}\ {\bf viral-encoded}\ {\bf protein}.$
- 67. The method of claim 66, wherein the target **antigen** is an **HIV** regulatory protein.
- 69. The method of claim 65, wherein the **antibody** is an **antibody** capable of binding to the envelope glycoprotein.
- 70. The method of claim 61, wherein the target  ${\tt antigen}$  is a TAR element or a RRE sequence.
- 71. The method of claim 61, wherein the cell is an animal or bird cell.
- 72. The method of claim 71, wherein the cell is an animal cell.
- 73. The method of claim 72, wherein the cell is an animal or bird cell.
- 74. The method of claim 73, wherein the cell is an animal cell.
- 75. The method of claim 74, wherein the animal cell is a mammalian cell.
- 76. The method of claim 72, wherein the animal is a mammalian cell.
- 77. The method of claim 61, wherein said single chain **antibody** contains a linker between said single chain **antibody**'s variable light chain and variable heavy chain.
- 78. The method of claim 77, wherein said linker is SEQ ID NO:1.
- 79. A method for the intracellular binding of a target antigen, which comprises: (a) delivery of a nucleic acid segment containing a promoter operably linked to an antibody gene capable of binding to said target antigen, wherein the antibody expressed by said antibody gene does not have a secretory sequence, and wherein the antibody is a single chain antibody or a Fab'; (b) intracellular expression of said antibody in a form capable of binding to said target antigen; and (c) intracellular binding of said target antigen by said antibody.
- 80. The method of claim 79, wherein the  ${\bf antibody}$  expressed by the nucleic acid segment is a Fab'.
- 81. The method of claim 79, wherein the target antigen is a protein.
- 82. The method of claim 79, wherein the target **antigen** is a protein whose expression results in malignant cellular transformation.
- 83. The method of claim 82, wherein the target  ${\bf antigen}$  results in malignant transformation as a result of overexpression of the protein.
- $84.\ \mbox{The method of claim 79, wherein the target $$antigen$ is a viral-encoded protein.}$

- 85. The method of claim 84, wherein the viral encoded protein is an  ${\bf HIV}\ {\bf viral}\ {\bf -encoded}\ {\bf protein}\ .$
- 86. The method of claim 85, wherein the target  ${\tt antigen}$  is an  ${\tt HIV}$  regulatory protein.
- $87.\ \mbox{The method of claim }86,$  wherein the regulatory protein is the rev protein.
- 88. The method of claim 84, wherein the **antibody** is an **antibody** capable of binding to the envelope glycoprotein.
- $89.\ \mbox{The method of claim }84,$  wherein the target  $\mbox{antigen}$  is the  $\mbox{HIV}$  envelope gp160.
- 90. The method of claim 79, wherein the target  ${\bf antigen}$  is a TAR element or a RRE sequence.
- 91. The method of claim 79, wherein said single chain **antibody** contains a linker between said single chain **antibody's** variable light chain and variable heavy chain.
- 92. The method of claim 91, wherein said linker is SEQ ID NO:1.
- 93. A method for binding a target protein by an **antibody** inside a human cell at a specified location which comprises: (a) delivery to said cell of a nucleic acid segment encoding at least a variable light chain and a variable heavy chain of an **antibody** which will bind to said protein, wherein said nucleic acid segment also encodes a localization sequence, (b) intracellular expression of said **antibody** in a form capable of binding to said target protein, wherein said **antibody** is a single chain or Fab', (c) intracellular delivery of said **antibody** to a site directed by said localization sequence, and (d) intracellular binding of said target protein at said site.
- 94. The method of claim 93, wherein the localization sequence is selected from the group consisting of routing signals, sorting signals, retention signals, salvage signals, and membrane topology-stop transfer signals.
- 95. A method for the intracellular binding of a target antigen, comprising: (a) introducing a nucleic acid segment encoding at least the heavy chain variable sequence of an antibody operably linked to a promoter into an animal cell, wherein the antibody is selected from the group consisting of single domain heavy chain, single chain, and Fab'; (b) intracellular expression of said heavy chain variable sequence; and (c) intracellular binding of said target antigen by said heavy chain variable sequence.
- 96. The method of claim 95, wherein the nucleic acid segment encodes only the heavy chain of a Fab.
- 97. The method of claim 95, wherein the nucleic acid segment encodes only the heavy chain variable sequence.
- .98. A method for the intracellular binding of a target antigen, comprising: (a) delivery of a nucleic acid segment containing a promoter operably linked to an antibody gene encoding an antibody capable of binding to said target antigen wherein the antibody contains a secretory signal and further contains an intracellular retention sequence; (b) intracellular expression of an antibody encoded by said nucleic acid segment; and (c) intracellular binding of said target antigen by said antibody.
- $99.\ \,$  The method of claim  $98,\ wherein$  the intracellular retention sequence is an endoplasmic reticulum localization sequence.
- 100. The method of claim 98, wherein the antibody is a Fab.
- 101. The method of claim 98 wherein the **antibody** is an **antibody** to an **HIV** envelope glycoprotein.
- L52 ANSWER 13 OF 41 USPATFULL on STN
  1999:21891 Methods for producing members of specific binding pairs.
  Winter, Gregory Paul, Cambridge, United Kingdom
  Johnson, Kevin Stuart, Cambridge, United Kingdom
  Griffiths, Andrew David, Cambridge, United Kingdom
  Smith, Andrew John Hammond, Cambridge, United Kingdom
  Medical Research Council, London, England (non-U.S. corporation)Cambridge
  Antibody Technology Limited, Melbourn, England (non-U.S. corporation)
  US 5871907 19990216

APPLICATION: US 1994-150002 19940331 (8)

WO 1992-GB883 19920515 19940331 PCT 371 date 19940331 PCT 102(e) date

PRIORITY: GB 1991-10549 19910515

GB 1992-6318 19920324

DOCUMENT TYPE: Utility; Granted. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A method of producing specific binding pair (sbp) members comprising: (a) a first polypeptide chain comprising an antibody heavy chain variable domain and a second polypeptide chain comprising an antibody light chain variable domain, or (b) a first polypeptide chain comprising an antibody light chain variable domain and a second polypeptide chain comprising an antibody heavy chain variable domain; which method comprises introducing into host cells (i) first vectors comprising nucleic acid encoding a genetically diverse population of said first polypeptide chain fused to a component of a secreted replicable genetic display package (rgdp) for display of said first polypeptide chains at the surface of rgdps, and (ii) second vectors comprising nucleic acid encoding a genetically diverse population of said second polypeptide chain; said first vectors being packaged in infectious rdgps and said introducing of said first vectors into host cells being by infection into host cells harboring said second vectors, or said second vectors being packaged in infectious rgdps and said introducing of said second vectors into host cells being by infection into host cells harboring said first vectors; and expressing said first and second polypeptide chains within the host cells to form a library of said sbp members displayed by rgdps, at least one of said population being expressed from nucleic acid that is packaged using rgdp component, whereby each said rgdp contains genetic material which encodes a polypeptide chain of the sbp member displayed at its surface.
- 2. A method according to claim 1 wherein at least one of said populations is expressed from a phage vector.
- 3. A method according to claim 1 wherein at least one of said populations is expressed from a phagemid vector, the method including using a helper phage or a plasmid expressing complementing phage genes, to help package said phagemid genome, and said component of the rgdp is a capsid protein therefore.
- 4. A kit for use in carrying out a method according to claim 1, said kit having the following components in addition to components required for carrying out the method: (i) a vector having the following features: (a) an origin of replication for single-stranded bacteriophage, (b) a restriction site for insertion of nucleic acid encoding or a polypeptide component of an sbp member, (c) said restriction site being in the 5' end region of the mature coding sequence of a phage capsid protein, and (d) with a secretory leader sequence upstream of said site which directs a fusion of the capsid protein and sbp polypeptide to the periplasmic space of a bacterial host; and (ii) another vector, having some or all of the features (a), (b), (c) and (d) of the vector described in (i).
- 5. A method according to claim 1 wherein each said first and second polypeptide chain is expressed from nucleic acid which is packaged as a rgdp using said component fusion product, whereby encoding nucleic acid for both said first and second polypeptide chains is packaged in respective rgdps.
- 6. A method according to claim 1 which comprises introducing vectors encoding a population of said first polypeptide chains into host organisms which express a population of said second polypeptide chains in free form, or introducing vectors encoding a population of said second polypeptide chains in free form into host organisms which express a population of said first polypeptide chains.
- 7. A method according to claim 1 wherein said second polypeptide chains are each expressed as a fusion with a component of a rgdp which thereby displays said second polypeptide chains at the surface of rgdps.
- 8. A method according to claim 1 wherein either or both of the populations of said first and second chains polypeptide chains is derived from a repertoire selected from the group consisting of: (i) the repertoire of rearranged immunoglobulin genes of an animal immunizéd with a complementary sbp member; (ii) the repertoire of rearranged immunoglobulin genes of an animal not immunized with a complementary sbp member; (iii) the repertoire of artificially rearranged immunoglobulin gene or genes; (iv) a repertoire of an immunoglobulin homolog gene or genes; (v) a repertoire of sequences derived from a germ-line immunoglobulin gene or genes; (vi) a repertoire of an immunoglobulin gene or genes artificially mutated by the introduction of one or more point mutations; and (vii) a mixture of any of (i), (ii), (iii), (iv),

- 9. A method according to claim 1 wherein said sbp members displayed by  $\operatorname{rgdps}$  are  $\operatorname{scFv}$  molecules.
- 10. A method according to claim 1 wherein the rgdp is a bacteriophage, the host is a bacterium, and said component of the rgdp is a **capsid** protein for the bacteriophage.
- $11.\ \mbox{A}$  method according to claim 10 wherein the phage is a filamentous phage.
- 12. The method according to claim 11 wherein the phage is selected from the group consisting of the class 1 phages, Fd, M13, f1, If1, Ike  $\rm ZJ/Z$ , Ff and the class II phages xf, Pf1 and Pf3.
- 13. A method according to claim 11 or claim 12 wherein the first polypeptide chains are expressed as fusions with the gene III **capsid** protein of phage fd or its counterpart in another filamentous phage.
- 14. A method according to claim 13 wherein the first polypeptide chains are each inserted in the N-terminal region of the mature **capsid** protein downstream of a secretory leader peptide.
- 15. A method according to claim 10 wherein the host is E. coli.
- 16. A method according to claim 1 wherein rgdps formed by said expression are selected or screened to provide an individual sbp member or a mixed population of said sbp members associated in their respective rgdps with nucleic acid encoding a polypeptide chain thereof.
- 17. A method of preparing an individual specific binding pair member, a mixed population of specific binding pair member, or polypeptide chain components thereof comprising the steps of: (i) obtaining nucleic acid from one or more rgdps produced by a method according to claim 16; and (ii) producing by expression from the nucleic acid obtained in step (i) an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof.
- 18. A method of preparing nucleic acid encoding an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof comprising the steps of: (i) obtaining nucleic acid from one or more rgdps produced by a method according to claim 16; and (ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof.
- 19. A method according to claim 16 wherein the rgdps are selected by affinity with a member complementary to said sbp member.
- 20. A method according to claim 19 which comprises recovering any rgdps bound to said complementary sbp member by washing with an eluant.
- 21. A method according to claim 19 wherein the rgdp is applied to said complementary sbp member in the presence of a molecule which competes with said package for binding to said complementary sbp member.
- 22. A method according to claim 20 wherein the eluant contains a molecule which compete with said rgdp for binding to the complementary sbp member.
- 23. A method according to any one of claims 16 or 19-22 wherein nucleic acid derived from a selected or screened rgdp is used to express said sbp member or a fragment or derivative thereof in a recombinant host organism.
- 24. A method of producing one or a selected population of multichain polypeptide members of a specific binding pair (sbp members) comprising: (a) a first polypeptide chain comprising an antibody heavy chain variable domain and a second polypeptide chain comprising an antibody light chain variable domain, or (b) a first polypeptide chain comprising an antibody light chain variable domain and a second polypeptide chain comprising an antibody heavy chain variable domain, and specific for a counterpart specific binding pair member of interest, which method comprises: (i) introducing into host cells (A) first vectors comprising nucleic acid encoding a genetically diverse population of said first polypeptide chain fused to a component of a secreted replicable genetic display package (rgdp) for display of said first polypeptide chains at the surface of rgdps, and (B) second vectors comprising nucleic acid encoding a unique or restricted population of said second polypeptide chain; said first vectors being packaged in infectious rgdps and said introducting of said first vectors into host cells being by infection

and none outly narrotting data bedona receptly of base become recept being packaged in infectious rgdps and said introducing of said second vectors into host cells being by infection into host cells harboring said first vectors; (ii) expressing said first and second polypeptide chains within the host cells to form a library of said multichain sbp members displayed by rgdps, said genetically diverse population of first polypeptide chains being expressed from nucleic acid that is packaged using said rgdp component, whereby each said rgdp contains genetic material which encodes a first polypeptide chain of the sbp member displayed at its surface; (iii) selecting by affinity with said counterpart sbp member of interest multichain sbp members specific for said counterpart sbp member associated in their respective rgdps with nucleic acid encoding a said first polypeptide chain of said multichain sbp members; (iv) combining said first polypeptide chains of multichain sbp members selected in step (iii) with a genetically diverse population of second polypeptide chains of multichain sbp members, the said second polypeptide chains being fused to a component of a rgdp which thereby displays them at the surface of rgdps, the said combining forming a library of multichain sbp members from which one or more multichain sbp members for said counterpart sbp member of interest are selectable by affinity with said counterpart sbp member of interest.

- 25. A method according to claim 24 wherein said selectable sbp members are  $\operatorname{scFv}$  molecules.
- 26. A method according to claim 25 wherein nucleic acid encoding a said first or second polypeptide chain is linked downstream to a viral capsid protein through a suppressible translational stop codon.
- 27. A method according to claim 24 wherein said multichain sbp members are antibodies, or other members of the immunoglobulin family, or binding fragments thereof.
- 28. A method according to claim 27 comprising an additional step 5 wherein humanized antibodies for said **antigen** are selected by affinity with said **antigen**.
- 29. A method according to claim 27 wherein each of said second polypeptide chains of steps (i) and (ii) comprises a variable domain derived from a non-human animal **antibody** specific for the **antigen** of interest.
- 30. A method according to claim 29 wherein said second polypeptide chains of (i) and (ii) are chimaeric, comprising a human **antibody** domain.
- 31. A method according to claim 30 wherein said human  ${\bf antibody}$  domain comprises Cy1.

## L52 ANSWER 14 OF 41 USPATFULL on STN

1999:4325 Methods for producing members of specific binding pairs.
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APPLICATION: US 1995-480006 19950607 (8)

PRIORITY: WO 1992-GB883 19920515

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

US 5858657 19990112

1. A method of producing specific binding pair (sbp) members comprising a first polypeptide chain and a second polypeptide chain, which method comprises: introducing into host cells; (i) first vectors comprising nucleic acid encoding a genetically diverse population of said first polypeptide chain fused to a component of a secreted replicable genetic display package (rgdp) for display of said polypeptide chains at the surface of rgdps; and (ii) second vectors comprising nucleic acid encoding a genetically diverse population of said second polypeptide chain; said first vectors being packaged in infectious rgdp's and their introduction into host cells being by infection into host cells harboring said second vectors; or said second vectors being packaged in infectious rgdp's and their introducing into host cells being by infection into host cells harboring said first vectors; and expressing said first and second polypeptide chains within the host cells to form a library of said sbp members displayed by rgdps, at least one of said populations being expressed from nucleic acid that is capable of being packaged using said rgdp component, whereby the genetic materials of each said rgdp encodes a polypeptide chain of the sbp member displayed at its surface.

- 2. A method according to claim 1 wherein at least one of said populations is expressed from a phage vector.
- 3. A method according to claim 1 or claim 2 wherein at least one of said populations is expressed from a phagemid vector, the method including using a helper phage or a plasmid expressing complementing phage genes, to help package said phagemid genome, and said component of the rgdp is a **capsid** protein therefore.
- 4. A method according to claim 1 wherein either or both of the populations of said first and second chains polypeptide chains is derived from a repertoire selected from the group consisting of: (i) the repertoire of rearranged immunoglobulin genes of an animal immunized with a complementary sbp member; (ii) the repertoire of rearranged immunoglobulin genes of an animal not immunized with a complementary sbp member; (iii) the repertoire of artificially rearranged immunoglobulin gene or genes; (iv) a repertoire of an immunoglobulin homolog gene or genes; (v) a repertoire of sequences derived from a germ-line immunoglobulin gene or genes; (vi) a repertoire of an immunoglobulin gene or genes artificially mutated by the introduction of one or more point mutations; and (vii) a mixture of any of (i), (ii), (iii), (iv), (v) and (vi).
- 5. A method according to claim 1 wherein each said first and second polypeptide chain is expressed from nucleic acid which is packaged as a rgdp using said component fusion product, whereby encoding nucleic acid for both said first and second polypeptide chains is packaged in respective rgdps.
- 6. A method according to claim 1 which comprises introducing vectors encoding a population of said first polypeptide chains into host organisms which express a population of said second polypeptide chains in free form, or introducing vectors encoding a population of said second polypeptide chains in free form into host organisms which express a population of said first polypeptide chains.
- 7. A method according to claim 1 wherein said second polypeptide chains are each expressed as a fusion with a component of a rgdp which thereby displays said second polypeptide chains at the surface of rgdps.
- 8. A method according to claim 1 wherein nucleic acid encoding a said first or second polypeptide chain is linked downstream to a viral **capsid** protein through a suppressible translational stop codon.
- 9. A method according to claim 1 wherein the rgdp is a bacteriophage, the host is a bacterium, and said component of the rgdp is a **capsid** protein for the bacteriophage.
- 10. A method according to claim 9 wherein the phage is a filamentous phage.
- 11. The method according to claim 10 wherein the phage is selected from the group consisting of the class 1 phages, Fd, M13, f1, If1, Ike,  $\rm ZJ/Z$ , Ff and the class II phages xf, Pf1 and Pf3.
- 12. A method according to claim 10 wherein the first polypeptide chains are expressed as fusions with the gene III **capsid** protein of phage fd or its counterpart in another filamentous phage.
- 13. A method according to claim 12 wherein the first polypeptide chains are each inserted in the N-terminal region of the mature **capsid** protein downstream of a secretory leader peptide.
- 14. A method according to claim 9 wherein the host is E.coli.
- 15. A method according to claim 1 wherein rgdps formed by said expression are selected or screened to provide an individual sbp member or a mixed population of said sbp members associated in their respective rgdps with nucleic acid encoding a polypeptide chain thereof.
- 16. A method according to claim 15 wherein the rgdps are selected by affinity with a member complementary to said sbp member.
- 17. A method according to claim 16 which comprises recovering any rgdps bound to said complementary sbp member by washing with an eluant.
- 18. A method according to claim 17 wherein the eluant contains a molecule which competes with said rgdp for binding to the complementary sbp member.
- 19. A method according to claim 16 wherein the rgdp is applied to said complementary sbp member in the presence of a molecule which competes

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- 20. A method according to claim 15 wherein nucleic acid derived from a selected or screened rgdp is used to express said sbp member or a fragment or derivative thereof in a recombinant host organism.
- 21. A method of preparing an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof comprising the steps of: (i) obtaining nucleic acid from one or more rgdps produced by a method according to claim 15; and (ii) producing by expression from the nucleic acid obtained in step (i) an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof.
- 22. A method of preparing nucleic acid encoding an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof comprising the steps of: (i) obtaining nucleic acid from one or more rgdps produced by a method according to claim 15; and (ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof.
- 23. A method of producing multimeric specific binding pair (sbp) members, which method comprises (i) causing or allowing intracellular recombination between (a) first vectors comprising nucleic acid encoding a population of a fusion of a first polypeptide chain of a specific binding pair member and a component of a secreted replicable genetic display package (rgdp) and (b) second vectors comprising nucleic acid encoding a population of a second polypeptide chain of a specific binding pair member, at least one of said populations being genetically diverse, the recombination resulting in recombinant vectors each of which comprises nucleic acid encoding a said polypeptide fusion and a said second polypeptide chain and capable of being packaged using said rgdp component; and (ii) expressing said polypeptide fusions and said second polypeptide chains, producing rgdps which display at their surface said first and second polypeptide chains and which each comprise nucleic acid encoding a said first polypeptide chain and a said second polypeptide chain.
- 24. A method according to claim 23 wherein the intracellular recombination is promoted by inclusion in the vectors of sequences at which site-specific recombination will occur.
- 25. A method according to claim 24 wherein said resultant recombinant vector comprises nucleic acid encoding a single chain Fv region derivative of an immunoglobulin resulting from recombination between first and second vectors.
- 26. A method according to claim 24 wherein the sequences at which site-specific recombination will occur are loxP sequences obtainable from coliphage P1, and site-specific recombination is catalysed by Cre-recombinase, also obtainable from coliphage P1.
- $27.\ \mbox{A}$  method according to claim 26 wherein the Cre-recombinase used is expressible under the control of a regulatable promoter.
- 28. A method according to claim 27 wherein said bacterial host is a PolA strain of E.coli or of another grain-negative bacterium.
- 29. A method according to claim 23 wherein the first vectors are phages or phagemids and the second vectors are plasmids, or the first vectors are plasmids and the second vectors are phages or phagemids, and the intracellular recombination takes place in a bacterial host which replicates plasmids preferentially over phages or phagemids, or which replicates phages or phagemids preferentially over plasmids.
- 30. A method according to claim 23 wherein nucleic acid from one or more rgdp's is taken and used in a further method to obtain an individual sbp member or a mixed population of sbp members, or polypeptide chain components thereof, or encoding nucleic acid therefor.
- 31. A method of producing one or a selected population of multichain polypeptide members of a specific binding pair (sbp members) specific for a counterpart specific binding pair member of interest, which method comprises the following steps: (i) expressing from a vector in recombinant host organism cells a genetically diverse population of a first polypeptide chain of said multichain protein, fused to a component of a replicable genetic display package (rgdp) which thereby displays said polypeptide chains at the surface of rgdps; (ii) combining said population with a unique or restricted population of second polypeptide chains of said multichain sbp members, not being expressed from the same vector as said population of first polypeptide chains, said combining

rorming a repract or para marcronari opp momero areprated by said genetically diverse population being expressed from nucleic acid which is capable of being packaged using said rgdp component, whereby the genetic material of each said rgdp encodes a said first polypeptide chain; (iii) selecting by affinity with said counterpart sbp member of interest multichain sbp members specific for said counterpart sbp member associated in their respective rgdps with nucleic acid encoding a said first polypeptide chain thereof; (iv) combining said first polypeptide chains of multichain sbp members selected in step (iii) with a genetically diverse population of second polypeptide chains of multichain sbp members, the said second polypeptide chains being fused to a component of a rgdp which thereby displays them at the surface of rgdps, the said combining in this step (iv) forming a library of multichain sbp members from which one or more multichain sbp members specific for said counterpart sbp member are selectable by affinity with it.

- 32. A method according to claim 31 wherein said multichain sbp members are antibodies, or other members of the immunoglobulin family, or binding fragments thereof.
- 33. A method according to claim 33 wherein each of said second polypeptide chains of steps (i) and (ii) comprises a variable domain derived from a non-human animal **antibody** specific for the **antigen** of interest.
- 34. A method according to claim 33 wherein said second polypeptide chains of steps (i) and (ii) are chimaeric, comprising a human antibody domain.
- 35. A method according to claim 34 wherein said human **antibody** domain comprises Cyl.
- 36. A method according to claim 32 comprising an additional step (v) wherein humanized antibodies for said **antigen** are selected by affinity with said **antigen**.
- 37. A method of producing one or a selected population of multichain polypeptide members of a specific binding pair (sbp members) comprising a first polypeptide chain and a second polypeptide chain, and specific for a counterpart specific binding pair member of interest; which method comprises: (i) introducing into host cells; (A) first vectors comprising nucleic acid encoding a genetically diverse population of said first polypeptide chain fused to a component of a secreted replicable genetic display package (rgdp) for display of said polypeptide chains at the surface of rgdps; and (B) second vectors comprising nucleic acid encoding a unique or restricted population of said second polypeptide chain; said first vectors being packaged in infectious rgdp's and their introduction into host cells being by infection into host cells harboring said second vectors; or said second vectors being packaged in infectious rgdp's and their introducing into host cells being by infection into host cells harboring said first vectors; (ii) expressing said first and second polypeptide chains within the host cells to form  $\boldsymbol{a}$ library of said multichain sbp members displayed by rgdps; said genetically diverse population of first polypeptide chains being expressed from nucleic acid that is capable of being packaged using said rgdp component, whereby the genetic material of each said rgdp encodes a first polypeptide chain of the sbp member displayed at its surface; (iii) selecting by affinity with said counterpart sbp member of interest multichain sbp members specific for said counterpart sbp member associated in their respective rgdps with nucleic acid encoding a said first polypeptide chain thereof; (iv) combining said first polypeptide chains of multichain sbp members selected in step (iii) with a genetically diverse population of second polypeptide chains of multichain sbp members, the said second polypeptide chains being fused to a component of a rgdp which thereby displays them at the surface of rgdps, the said combining in this step (iv) forming a library of multichain sbp members from which one or more multichain sbp members for said counterpart sbp member of interest are selectable by affinity with
- 38. A method according to claim 37 wherein rgdps formed by said expression are selected or screened to provide an individual sbp member or a mixed population of said sbp members associated in their respective rgdps with nucleic acid encoding a polypeptide chain thereof.
- 39. A method of preparing an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof comprising the steps of: (i) obtaining nucleic acid from one or more rgdps produced by a method according to claim 38; and (ii) producing by expression from the nucleic acid obtained in step (i) an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof.

40. A method of preparing nucleic acid encoding an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof comprising the steps of: (i) obtaining nucleic acid from one or more rgdps produced by a method according to claim 38; and (ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes an individual specific binding pair member, a mixed population of specific binding pair members, or polypeptide chain components thereof.

L52 ANSWER 15 OF 41 USPATFULL on STN 1998:134797 In vitro diagnostic assays for the detection of HIV-1 or HIV-2 employing viral-specific antigens and antibodies. Montagnier, Luc, Le Plessis Robinson, France Guetard, Denise, Paris, France Alizon, Marc, Paris, France Clavel, Fran.cedilla.ois, Paris, France Guyader, Mireille, Paris, France Sonigo, Pierre, Paris, France Institut Pasteur, Paris, France (non-U.S. corporation) US 5830641 19981103 APPLICATION: US 1994-214299 19940317 (8) PRIORITY: FR 1986-910 19860122 FR 1986-911 19860122 FR 1986-1635 19860206 FR 1986-1985 19860213 FR 1986-3881 19860318 FR 1986-4215 19860324 DOCUMENT TYPE: Utility; Granted. CAS INDEXING IS AVAILABLE FOR THIS PATENT. CLM What is claimed is:

- 1. An in vitro diagnostic assay for the detection of antibodies specific for human immunodeficiency virus type 1 (HIV-1), type 2 (HIV-2), or both types 1 and 2 in a biological sample, comprising: (a) contacting the biological sample with one or more HIV-2 peptides selected from the group consisting of: (1) a peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: #STR2## (2) a peptide encoded by the HIV-2 env gene, wherein said peptide comprises the following sequence: ##STR3## (3) a p16 peptide encoded by the **HIV-**2 gag gene, wherein said peptide comprises the following sequence: ##STR4## (4) a p26 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR5## (5) a pl2 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR6## (b) contacting said biological sample with one or more HIV-1 peptides; and (c) detecting the formation of antigen-antibody complexes between said one or more peptides and antibodies present in said biological sample.
- 2. The assay of claim 1, wherein said sample is also contacted with one or more proteins selected from the group consisting of external env glycoprotein of **HIV-**2 and transmembrane env protein of **HIV-**2.
- 3. The assay of claim 1, wherein said one or more peptides of **HIV-1** is selected from the group consisting of p25, p18, gp110, and gp41 of **HIV-1**.
- 4. The assay according to any one of claims 1, 2, or 3, wherein the formation of **antigen-antibody** complex is detected by employing a process selected from the group consisting of radioimmunoassay, radioimmunoprecipitation assay, immunofluorescence assay, enzyme-linked immunosorbent assay, and Western blot.
- 5. The assay according to claim 4, wherein said peptide or protein is labeled with a label selected from the group consisting of an enzyme label, a fluorescent label, and a radioactive label.
- 6. An in vitro diagnostic kit for the detection of antibodies specific for human immunodeficiency virus type 1 (HIV-1), type 2, or both type 1 and 2 in a biological sample, comprising: (a) a peptide composition comprising one or more HIV-2 peptides selected from the group consisting of: (1) a peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR7## (2) a peptide encoded by the  ${\bf HIV}\text{--}2$  env gene, wherein said peptide comprises the following sequence: ##STR8## (3) a pl6 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR9## (4) a **p26** peptide encoded by the **HIV-2** gag gene, wherein said peptide comprises the following sequence: ##STR10## (5) a p12 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR11## (b) a peptide composition comprising one or more HIV-1 peptides; and (c) reagents for the detection of antigen-antibody complex formation between said one or more peptides and antibodies present in said biological sample.

- 7. The kit of claim 6, further comprising a peptide composition having one or more peptides selected from the group consisting of external env glycoprotein of **HIV-2** and transmembrane env protein of **HIV-2**.
- 8. The kit of claim 6, wherein said one or more peptides of  ${\tt HIV-1}$  is selected from the group consisting of p25, p18, gp110, and gp41 of  ${\tt HIV-1}$ .
- 9. The kit according to any one of claims 6, 7, or 8, wherein said peptide or protein is labeled with a label selected from the group consisting of an enzyme label, a fluorescent label, and a radioactive label.
- 10. An in vitro diagnostic assay for the detection of antigens of human immunodeficiency virus type 1, type 2, or both types 1 and 2 in a biological sample, comprising: (a) contacting the biological sample with one or more antibodies against an HIV-2 peptide selected from the group consisting of: (1) an antibody specific for a peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR12## (2) an **antibody** specific for a peptide encoded by the HIV-2 env gene, wherein said peptide comprises the following sequence: ##STR13## (3) an antibody specific for a p16 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR14## (4) an antibody specific for a p26 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR15## (5) an antibody specific for a p12 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR16## (b) contacting said biological sample with one or more antibodies specific for an HIV-1 peptide; and (c) detecting the formation of antigen-antibody complexes between said one or more antibodies and antigens present in said biological sample.
- 11. The assay of claim 10, wherein said sample is also contacted with one or more antibodies selected from the group consisting of **antibody** specific for the external **HIV-**2 env glycoprotein and **antibody** specific for the transmembrane **HIV-**2 env protein.
- 12. The assay of claim 10, wherein said one or more antibodies specific for an HIV-1 peptide are selected from the group consisting of antibody specific for HIV-1 p25, antibody specific for HIV-1 p18, antibody specific for HIV-1 gp110, and antibody specific for HIV-1 gp41.
- 13. The assay according to any one of claims 10, 11, and 12, wherein the formation of **antigen-antibody** complex is detected by employing a process selected from the group consisting of radioimmunoassay, radioimmunoprecipitation assay, immunofluorescence assay, enzyme-linked immunosorbent assay, and Western blot.
- 14. An in vitro diagnostic kit for the detection of antigens of a human immunodeficiency virus type 1, type 2, or both types 1 and 2
  in a biological sample, comprising: (a) an antibody composition comprising one or more antibodies specific for an HIV-2 peptide selected from the group consisting of: (1) an antibody specific for a peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR17## (2) an antibody specific for a peptide encoded by the HIV-2 env gene, wherein said peptide comprises the following sequence: ##STR18## (3) an antibody specific for a p16 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR19## (4) an antibody specific for a p26 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR20## (5) an antibody specific for a pl2 peptide encoded by the HIV-2 gag gene, wherein said peptide comprises the following sequence: ##STR21## (b) an antibody composition comprising one or more antibodies specific for an HIV-1 peptide; and (c) reagents for the detection of antigen-antibody complex formation between said one or more antibodies and antigens present in said biological sample.
- 15. The kit of claim 14, further comprising an **antibody** composition having one or more antibodies selected from the group consisting of **antibody** specific for the **HIV-**2 external env glycoprotein and **antibody** specific for the **HIV-**2 transmembrane env protein.
- 16. The kit of claim 14, wherein said one or more antibodies specific for an HIV-1 peptide are selected from the group consisting of antibody specific for HIV-1 p25, antibody specific for HIV-1 p18, antibody specific for HIV-1 gp110, and antibody specific for HIV-1 gp41.
- 17. The diagnostic assay of any one of claims 1-5, wherein said  ${\bf HIV-2}$  peptides and proteins are specific for  ${\bf HIV-2}_{ROD}$  and wherein said

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- 18. The diagnostic kit of any one of claims 6-9, wherein said  ${\bf HIV}$ -2 peptides and proteins are specific for  ${\bf HIV}$ -2 $_{{\bf ROD}}$  and wherein said  ${\bf HIV}$ -1 peptides are specific for  ${\bf HIV}$ -1 $_{{\bf BRU}}$ .
- 19. The diagnostic assay of any one of claims 10-12, wherein said  ${\bf HIV-2}$  peptides and proteins are specific for  ${\bf HIV-2}_{ROD}$  and wherein said  ${\bf HIV-1}$  peptides are specific for  ${\bf HIV-1}_{BRU}$ .
- 20. The diagnostic assay of any one of claims 14-16, wherein said  ${\bf HIV-2}$  peptides and proteins are specific for  ${\bf HIV-2}_{ROD}$  and wherein said  ${\bf HIV-1}$  peptides are specific for  ${\bf HIV-1}_{BRU}$ .
- 21. The diagnostic assay of claim 1, wherein said contacting steps occur simultaneously.
- 22. The diagnostic assay of claim 6, wherein said contacting steps occur simultaneously.
- 23. The diagnostic assay of claim 10, wherein said contacting steps occur simultaneously.
- 24. The diagnostic assay of claim 14, wherein said contacting steps occur simultaneously.
- L52 ANSWER 16 OF 41 USPATFULL on STN
- 97:54076 Method for measuring anti-HIV-1 p24 antibody and use thereof. Povolotsky, Jacob L., Brooklyn, NY, United States Polsky, Bruce W., New York, NY, United States Armstrong, Donald, New York, NY, United States Sloan-Kettering Institute for Cancer Research, New York, NY, United States (U.S. corporation)
  US 5641624 19970624

APPLICATION: US 1994-253114 19940602 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A method for measuring the amount of anti-HIV-1 p24 antibody obtained from a suitable bodily fluid sample from an HIV-1-infected subject which comprises: (a) contacting a predetermined amount of immobilized anti-HIV-1 p24 antibody with a known nonsaturating amount of HIV-1 p24 antigen under conditions permitting binding of the HIV-1 p24 antigen to the immobilized anti-HIV-1 p24 antibody so as to form a first complex; (b) removing any unbound HIV-1 p24 antigen; (c) contacting the bodily fluid sample with the first complex under conditions permitting binding of anti-HIV-1 p24 antibody in the sample to the first complex so as to form a second complex; (d) removing any unbound anti-HIV-1 p24 antibody; (e) contacting the second complex with a labeled antibody which specifically binds to any HIV-1 p24 antigen not present in the second complex; (f) removing any unbound labeled antibody; and (g) quantitatively determining the amount of labeled antibody bound to HIV-1 p24 antigen so as to thereby quantitatively determine the amount of anti-HIV-1 p24 antibody present in the second complex.
- 2. The method of claim 1, wherein the bodily fluid sample is selected from the group consisting of serum, plasma, cerebrospinal fluid, sperm, sputum and urine.
- 4. The method of claim 1, wherein before step (c) the bodily fluid sample is treated with base.
- 5. The method of claim 1, wherein before step (c) the bodily fluid is serially diluted.
- 6. The method of claim 1, wherein the subject is a human.
- 7. A method for determining the progression of an HIV-1 infection in a subject which comprises: (a) obtaining at least two suitable bodily fluid samples from the subject at different times; (b) measuring the amount of anti-HIV-1 p24 antibody present in each such sample according to the method of claim 1; and (c) determining the difference between the amounts of anti-HIV-1 p24 antibody measured in such samples so as to thereby determine the progression of the HIV-1 infection in the subject.
- 8. A method for determining the efficacy of a drug for treating a subject infected with **HIV-1** which comprises: (a) obtaining at least

after the drug has been administered to the subject; and (b) measuring the amount of anti-HIV-1 p24 antibody present in each such sample according to the method of claim 1 so as determine the efficacy of the drug.

L52 ANSWER 17 OF 41 USPATFULL on STN
97:7798 Cell fixative and method of analyzing virally infected cells.
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US 5597688 19970128

APPLICATION: US 1995-467799 19950606 (8)

DOCUMENT TYPE: Utility; Granted.

CLM What is claimed is:

- 1. A method for monitoring human immunodeficiency virus (HIV) infection in a patient so infected, comprising the steps of: a) contacting a sample of whole blood from said patient with a fixative composition in an amount and for a period of time effective to fix white blood cells present in said whole blood, without substantially destroying the ability of white blood cell antigens and viral components to bind ligands, wherein said fixative composition comprises: i) a first fixative compound selected from the group consisting of 2,4-dinitrobenzene sulfonic acid, 2,4-dinitrobenzoic acid, 2,4-dinitrophenol, and a combination of two or more of these; ii) a second fixative compound which is methanol-free, high-grade formaldehyde in a concentration ranging from about 0.1% to about 4%; iii) dimethyl<br/>sulfoxide in a concentration of about 1% (v/v) to about 20% (v/v); and iv) a polyoxyethylene sorbitan surfactant in a concentration of about 0.001% to about 0.2% (w/v); b) isolating white blood cells present in said sample; c) either concurrently with the contact Step in a) or thereafter, contacting the cells so fixed with at least one antibody to a white blood cell antigen and at least one binding ligand that binds to at least one component from HIV; d) examining the scattering and fluorescent properties of said cells so fixed with a flow cytometer; and e) comparing the results of said examination to data obtained in the same manner from patients at various stages of HIV infection.
- 2. The method of claim 1 wherein said first fixative compound is 2,4-dinitrobenzene sulfonic acid.
- 3. The method of claim 1 wherein said at least one binding ligand that binds to said component from **HIV** is anti-p24 antibody.
- 4. The method of claim 1 wherein said at least one antibody to a white blood cell antigen is an anti-CD4 monoclonal antibody.
- 5. The method of claim 4 wherein said anti-CD4 monoclonal **antibody** is labelled with phycoerythrin and said anti-**p24 antibody** is labelled with FITC.
- 6. A reagent kit for monitoring HIV load in HIV-infected white blood cells, comprising: a) a fixative composition which comprises: i) a first fixative compound selected from the group consisting of 2,4-dinitrobenzene sulfonic acid, 2,4-dinitrobenzoic acid, 2,4-dinitropenzol, and a combination of two or more of these; ii) a second fixative compound which is methanol-free, high-grade formaldehyde in a concentration ranging from about 0.1% to about 4%; iii) dimethylsulfoxide in a concentration of about 1% (v/v) to about 20% (v/v); and iv) a polyoxyethylene sorbitan surfactant in a concentration of about 0.001% to about 0.2% (w/v); and b) a binding ligand that binds to an intracellular antigen from HIV.
- 7. The reagent kit of claim 6 further comprising at least one **antibody** to a white blood cell surface **antigen**.
- 8. The reagent kit of claim 7 wherein at least one of said antibodies to a white blood cell surface antigen is a monoclonal antibody to CD4 positive T cells.
- 9. The reagent kit of claim 8 further comprising at least one monoclonal  ${\bf antibody}$  to monocytes.

L52 ANSWER 18 OF 41 USPATFULL on STN
96:111330 Peptides of human immunodeficiency virus type 2 (HIV-2) and in vitro diagnostic methods and kits employing the peptides for the detection of HIV-2.

Alizon, Marc, Paris, France

.....ug..zoz, zuo, zo rzoodzo nodznoch, rzunoc Geutard, Denise, Paris, France Clavel, Francois, Rockville, MD, United States Sonigo, Pierre, Paris, France Guyader, Mireille, Paris, France Institut Pasteur, Paris, France (non-U.S. corporation) US 5580739 19961203 APPLICATION: US 1994-214221 19940317 (8) PRIORITY: FR 1986-911 19860122 FR 1986-1635 19860206 FR 1986-1985 19860213 FR 1986-3881 19860318 FR 1986-4215 19860324 DOCUMENT TYPE: Utility; Granted. CAS INDEXING IS AVAILABLE FOR THIS PATENT. What is claimed is: CLM

- 1. A peptide comprising the gag precursor protein of human
  immunodeficiency virus type 2 (HIV-2<sub>ROD--</sub>), wherein the
  peptide is free of particles of said virus, having the following amino
  acid sequence: ##STR4##
- 2. A peptide comprising the polymerase precursor protein of **human immunodeficiency virus** type 2 (**HIV**- $2_{ROD}$ ), wherein the peptide is free of particles of said virus, having the following amino acid sequence: ##STR5##
- 3. A peptide comprising the Vif protein of **human immunodeficiency virus** type 2 (**HIV**-2<sub>ROD--</sub>), wherein the peptide is free of particles of said virus, having the following amino acid sequence: ##STR6##
- 4. A peptide comprising the Vpr protein of **human immunodeficiency virus** type 2 (**HIV**-2<sub>ROD--</sub>), wherein the peptide is free of particles of said virus, having the following amino acid sequence: ##STR7##
- 5. A peptide comprising the Vpx protein of **human immunodeficiency virus** type 2 (**HIV**- $2_{ROD}$ ), wherein the peptide is free of particles of said virus, having the following amino acid sequence: ##STR9##
- 6. A peptide comprising the Nef protein of **human immunodeficiency virus** type 2 (**HIV**-2<sub>ROD</sub>), wherein the peptide is free of particles of said virus, having the following amino acid sequence: ##STR9##
- 7. A peptide comprising the TAT protein of **human immunodeficiency virus** type 2 (**HIV**-2<sub>ROD</sub>), wherein the peptide is free of particles of said virus, having the following amino acid sequence: ##STR10##
- 8. A peptide comprising the Rev protein of **human immunodeficiency virus** type 2 ( $HIV-2_{ROD--}$ ), wherein the peptide is free of particles of said virus, having the following amino acid sequence: #STR11#
- 9. An in vitro diagnostic method for the detection of the presence or absence of antibodies which bind to antigens of a human immunodeficiency virus type 2 (HIV-2) comprising: (a) contacting a biological sample with one or more peptides selected from the group consisting of: (1) a peptide comprising the gag precursor protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD--</sub>), having the following sequence: ##STR12## (2) a peptide comprising the polymerase precursor protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR13## (3) a peptide comprising the env precursor protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR14## (4) a peptide comprising the Vif protein of human immunodeficiency virus type 2 (HIV- $2_{\text{ROD}}$ ), having the following sequence: ##STR15## (5) a peptide comprising the Vpr protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR16## (6) a peptide comprising the Vpx protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR17## (7) a peptide comprising the Nef protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR18## (8) a peptide comprising the TAT protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR19## (9) a peptide comprising the Rev protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: #STR20# (10) a peptide comprising the pl6/matrix protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the

p26/capsid protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR22## (12) a peptide comprising the p12/nucleocapsid protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR23## (b) detecting the formation of antigen-antibody complex between said one or more peptides and antibodies present in said biological sample: and (c) providing a biological reference sample lacking antibodies recognized by said one or more peptides, wherein the one or more peptides and the biological reference sample are present in an amount sufficient to perform the detection of antigen-antibody complex formed between said one or more peptides and antibodies present in the biological sample, said detection being indicative of previous exposure to HIV-2.

- 10. The method of claim 9, wherein the formation of antigen-antibody complex is detected by employing a process selected from the group consisting of radioimmunoassay, radioimmunoprecipitation assay, immunofluorescence assay, enzyme-linked immunosorbent assay, and Western blot.
- 11. An in vitro diagnostic method for the detection of the presence or absence of antibodies which bind to antigens of a human immunodeficiency virus type 2 (HIV-2) comprising: (a) contacting a biological sample with a peptide comprising the Nef protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR24## (b) detecting the formation of antigen-antibody complex between said peptide and antibodies present in said biological sample; and (c) providing a biological reference sample lacking antibodies recognized by said peptide. wherein the peptide and the biological reference sample are present in an amount sufficient to perform the detection of antigen-antibody complex formed between said peptide and antibodies present in the biological sample, said detection being indicative of previous exposure to HIV-2.
- 12. The method of claim 11, wherein the formation of antigen-antibody complex is detected by employing a process selected from the group consisting of radioimmunoassay, radioimmunoprecipitation assay, immunofluorescence assay, enzyme-linked immunosorbent assay, and Western blot.
- 13. A diagnostic kit for the in vitro detection of the presence or absence of antibodies which bind to antigens of a human immunodeficiency virus type 2 (HIV-2) comprising: (a) a peptide composition comprising one or more peptides selected from the group consisting of: (1) a peptide comprising the gag precursor protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR25## (2) a peptide comprising the polymerase precursor protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR26## (3) a peptide comprising the env precursor protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR27## (4) a peptide comprising the Vif protein of human immunodeficiency virus type 2 (HIV- $2_{\text{ROD}}$ ), having the following sequence: ##STR28## (5) a peptide comprising the Vpr protein of human immunodeficiency virus type 2 (HIV-2ROD), having the following sequence: ##STR29## (6) a peptide comprising the Vpx protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR30## (7) a peptide comprising the Nef protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR31## (8) a peptide comprising the TAT protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR32## (9) a peptide comprising the Rev protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR33## (10) a peptide comprising the pl6/matrix protein of human immunodeficiency virus type 2 (HIV- $2_{\text{ROD}}$ ), having the following sequence: ##STR34## (11) a peptide comprising the p26/capsid protein of human immunodeficiency virus type 2 (HIV-2<sub>ROD</sub>), having the following sequence: ##STR35## (12) a peptide comprising the pl2/nucleocapsid protein of human immunodeficiency virus type 2 (HIV- $2_{ROD}$ ), having the following sequence: ##STR36## (b) reagents for the detection of the formation of antigen-antibody complex; and (c) a biological reference sample lacking antibodies recognized by said peptide composition, wherein the peptide composition, reagents, and biological reference sample are present in an amount sufficient to perform the detection of antigen-antibody complex formed between said one or more peptides and antibodies present in the biological sample, said detection being indicative of previous exposure to HIV-2.
- 14. A diagnostic kit for the in vitro detection of the presence or

immunodeficiency virus type 2 (HIV-2) comprising: (a) a peptide having the following sequence: ##STR37## (b) reagents for the detection of the formation of antigen-antibody complex; and (c) a biological reference sample lacking antibodies recognized by said peptide; wherein the peptide, reagents, and biological reference sample are present in an amount sufficient to perform the detection of antigen-antibody complex formed between said peptide and antibodies present in the biological sample, said detection being indicative of previous exposure to HIV-2.

L52 ANSWER 19 OF 41 USPATFULL on STN

96:87359 HIV immunotherapeutics.
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Nissin Shokuhin Kabushiki Kaisha, Osaka, Japan (non-U.S. corporation) US 5558865 19960924

APPLICATION: US 1993-111080 19930824 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. An NM01 monoclonal **antibody** characterized by the ability to specifically bind to the amino acids G-P-G-R (SEQ ID NO: 1) of HIV-1 gpl20 or gpl60 protein and the ability to neutralize in vitro the infection of H9 cells by live HIV-1 strains MN and  $III_B$  as determined by reverse transcriptase, **p24**. MT-2 and syncytia formation assays, the **antibody** being further characterized by comprising a heavy chain variable region consisting of the amino acid sequence set out in SEO ID NO: 20 and a light chain variable region consisting of the amino acid sequence set out in SEQ ID NO: 22.
- 2. An NM01 monoclonal **antibody** characterized by the ability to specifically bind amino acids G-P-G-R (SEQ ID. No:1) of **HIV**-1 gp120 or gp160 protein and the ability to neutralize in vitro infection of H9 cells by live **HIV**-1 strains MN and III $_{\rm B}$  as determined by reverse transcriptase, **p24**, MT-2 and syncytia formation assays.
- 3. The  ${\bf antibody}$  of claim 1 or claim 2 which is produced by hybridoma cell line ATCC HB 10726.
- 4. The  ${\bf antibody}$  of claim 1 or claim 2 comprising murine NMO1 variable regions and human constant regions.
- 5. A CDR-grafted antibody comprising the complementarity determining regions of the antibody of claim 1 or claim 2.
- 6. An **antibody** fragment which retains the **antigen**-binding properties of the NM01 **antibody** of claim 1 or claim 2, wherein said **antibody** fragment is selected from the group consisting of a Fab fragment and a F(ab')2 fragment.
- $7.\ \mbox{A composition comprising the $antibody}$ of claim 1 or claim 2 and an acceptable carrier.$
- 8. Hybridoma cell line ATCC HB 10726.

L52 ANSWER 20 OF 41 USPATFULL on STN

96:38768 T-lymphotropic retrovirus monoclonal antibodies.

Butman, Bryan T., Walkersville, MD, United States Venetta, Thomas M., Derwood, MD, United States Akzo Nobel N.V., Arnhem, Netherlands (non-U.S. corporation) US 5514541 19960507

APPLICATION: US 1994-304977 19940913 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A monoclonal **antibody** that cross-reacts with an epitope of **p24** of **HIV-1** and **p26** of **HIV-2**, said epitope located within amino acid residues 142-158 of **p24** based on the numbering depicted in FIG. 9.
- 2. A diagnostic kit for the detection of HIV-1 and HIV-2, comprising: (1) a container containing the monoclonal antibody of claim 1; and (2) a container containing a labeled anti-HIV antibody that can detect immunocomplexes of the monoclonal antibody and the antigen of at least one of HIV-1 and HIV-2.
- 3. The diagnostic kit of claim 1, further comprising an additional monoclonal **antibody** that reacts with an **antigen** of **HIV-1**, wherein said additional monoclonal **antibody** does not react with said epitope of claim 1.
- 4. The diagnostic kit of claim 3, wherein said additional monoclonal

located within amino acid residues 263-344 of p24.

- 5. A method for detection of HIV-1 and HIV-2 antigens in a sample, comprising contacting said sample with the monoclonal **antibody** of claim 1, and measuring the formation of **antigen-antibody** complexes.
- 6. The method of claim 5, further comprising contacting the sample with an additional monoclonal **antibody** that has reactivity with an epitope of **HIV-**1 other than the epitope of the monoclonal **antibody** of claim 5, prior to measuring the formation of **antigen-antibody** complexes.
- 7. The method of claim 6, wherein the additional monoclonal **antibody** binds with an epitope located within amino acid residues 263-344 of **p24**, based on the numbering depicted in FIG. 5.
- 8. A method for detection of HIV-1 and HIV-2 antigens in a sample, which comprises contacting said sample with the monoclonal antibody of claim 1, and an additional antibody that reacts with an antigen of HIV-1 or HIV-2 but does not react with the epitope to which the monoclonal antibody of claim 1 reacts, and measuring the formation of antigen-antibody complexes.
- 9. A monoclonal  ${\bf antibody}$  according to claim 1, wherein said monoclonal  ${\bf antibody}$  is 7-D4.
- 10. A cell line for producing the monoclonal **antibody** according to claim 9, having ATCC Accession Number HB 11254.
- 11. The diagnostic kit of claim 2, wherein said monoclonal  ${\bf antibody}$  is monoclonal  ${\bf antibody}$  7-D4.
- 12. The method of claim 8, comprising contacting the sample with the monoclonal  ${\bf antibody}\ {\bf 7-D4}\,.$
- L52 ANSWER 21 OF 41 USPATFULL on STN
- 95:80210 Protein-dye conjugate for confirmation of correct dilution of calibrators.

Meiklejohn, Bruce, San Diego, CA, United States Chiapetta, Michael, San Marcos, CA, United States Hybritech Incorporated, San Diego, CA, United States (U.S. corporation) US 5447838 19950905

APPLICATION: US 1992-925513 19920805 (7)

DOCUMENT TYPE: Utility; Granted. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A composition for facilitating a determination that a stock solution  $% \left( 1\right) =\left( 1\right) \left( 1\right) \left($ containing a calibration or control material ("calibrator") dissolved therein has been diluted correctly, said composition comprising, a solution having dissolved therein: a) a first compound ("calibrator") designated for use in calibrating an assay for an analyte of interest over a working concentration range, said calibrator being the same or substantially the same as the analyte of interest, said calibrator being present in said solution at a concentration that is substantially above the working concentration range of said analyte of interest; and b) an identifiably effective and non-interfering amount of a second compound ("marker") dissolved therein substantially for identifying the dilution level of said stock solution over the working concentration range of said calibrator, said marker being a dye conjugated to a carrier protein, said marker having a concentration that is proportional to the concentration of said calibrator, said marker neither participating as a reactant nor as a label on a reactant in said assay for said analyte of
- 2.. The composition of claim 1 wherein the stock solution is an aqueous based solution.
- 3. The composition of claim 1 wherein the calibrator is a ligand or an antiligand.
- 4. The composition of claim 3 wherein the ratio of dye to carrier protein is within the range of about 1:1 to about 15:1.
- 5. The composition of claim 4 wherein the carrier protein is a mammalian serum protein.
- 6. The composition of claim 5 wherein the mammalian serum protein is selected from the group consisting of bovine serum albumin, human serum albumin, porcine serum albumin, sheep serum albumin, murine serum albumin, goat serum albumin, and guinea pig serum albumin.
- 7. The composition of claim 6 wherein the mammalian serum protein is

- 8. The composition of claim 7 wherein the dye absorbs light in the visible spectrum.
- 9. The composition of claim 8 wherein the calibrator is selected from the group consisting of prostate specific antigen, human bone alkaline phosphatase antigen, human chorionic gonadotropin, follicle stimulating hormone, human leutenizing hormone, creatine phosphokinase MB isoenzyme, ferritin, carcinoembryonic antigen, CA-549, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antigen, hepatitis B core antibody, hepatitis A virus antibody, hepatitis C virus antibody, the p41 antigen of HIV II, the gp120 antigen of HIV I, the p66 antigen of HIV I, the p41 antigen of HIV I, the p31 antigen of HIV I, the p24 antigen of HIV I, the p17 antigen of HIV I, and an antiligand to any one of said aforementioned antigens.
- 10. The composition of claims 1 or 8 wherein the dye is selected from the group consisting of Malachite Green, fluorescein, eosin, tetramethylrhodamine, phenolphthalein and erythrosin.
- 11. The composition of claim 10 wherein the dye is Malachite Green.
- 12. The composition of claim 11 wherein the ratio of dye to carrier protein is within the range from about 2.8:1 to about 7:1.
- 13. A series of calibrator solutions, each calibrator solution in said series having therein a predetermined concentration of a non-visible calibrator and an identifiably effective and non-interfering amount of a visible marker, said marker being a colored dye conjugated to a carrier protein, the amount of visible marker in each calibrator solution being proportional to the concentration of said calibrator, said series of calibrator solutions spanning a predetermined range of calibrator concentrations and a corresponding range of marker concentrations, whereby each solution in said series of calibrator solutions has a color intensity in proportion to the concentration of calibrator therein.
- 14. The series of calibrator solutions of claim 13 wherein the calibrator is a ligand or an antiligand.
- 15. The series of calibrator solutions of claim 14 containing from 2 to 10 calibrator solutions.
- 16. The series of calibrator solutions of claim 15 wherein one or more calibrator solutions in said series are capable of functioning as control solutions in an assay.
- 17. The calibrator solution of claims 13 or 16 wherein the calibrator is selected from the group consisting of human bone alkaline phosphatase antigen, human chorionic gonadotropin, human leutenizing hormone, human follicle stimulating hormone, ferritin, carcinoembryonic antigen, prostate specific antigen, CA-549, creatine kinase MB isoenzyme, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antigen, hepatitis B core antibody, hepatitis A virus antibody; hepatitis C virus antibody, the p41 antigen of HIV II, the gp120 antigen of HIV I, the p66 antigen of HIV I, the p41 antigen of HIV I, the p31 antigen of HIV I, the p42 antigen of HIV I, the p17 antigen of HIV I, and an antiligand to any one of said aforementioned antigens.
- $18.\$ The series of calibrator solutions of claim 16 wherein the colored dye is selected from the group consisting of Malachite Green, eosin and erythrosin.
- 19. The series of calibrator solutions of claim 18 wherein the carrier protein is a mammalian serum protein.
- $20.\ \,$  The series of calibrator solutions of claim 19 wherein the mammalian serum protein is a mammalian serum albumin.
- 21. The series of calibrator solutions of claim 20 wherein the mammalian serum albumin is selected from the group consisting of bovine serum albumin, human serum albumin, procine serum albumin, sheep serum albumin, murine serum albumin, goat serum albumin and guinea pig serum albumin.
- $22.\$ The series of calibrator solutions of claim 21 wherein the mammalian serum albumin is bovine serum albumin.
- 23. The series of calibrator solutions of claim 22 wherein the colored dye is Malachite Green.

dye to protein is within the range from about 2.8:1 to about 7:1.

- 25. A series of calibrator solutions for calibrating a diagnostic test kit, said series spanning a predetermined range of calibrator concentrations, each solution in said series having a predetermined concentration of calibrator therein and a second predetermined and non-interfering concentration of a colored marker therein, said marker being a colored dye conjugated to a carrier protein, said concentration of colored marker in each solution in said series being proportional to the concentration of calibrator therein, each solution in said series having a color intensity in proportion to the concentration of calibrator therein such that said series spans a range of color intensity in proportion to the range of calibrator concentrations therein.
- $26.\ \mbox{The series}$  of calibrator solutions of claim  $25\ \mbox{wherein}$  said working calibrator solutions are aqueous based.
- 27. The series of calibrator solutions of claim 26 wherein the calibrator is a ligand or an antiligand.
- 28. The series of calibrator solutions of claim 27 wherein the ratio of dye to carrier protein is within the range from about 1:1 to about 15:1.
- $29.\ \mbox{The series}$  of calibrator solutions of claim 28 wherein the carrier protein is a mammalian serum protein.
- 30. The series of calibrator solutions of claim 29 wherein the mammalian serum protein is selected from the group consisting of bovine serum albumin, human serum albumin, porcine serum albumin, sheep serum albumin, murine serum albumin, goat serum albumin, and guinea pig serum albumin.
- 31. The series of calibrator solutions of claims 23 or 25 wherein the calibrator is selected from the group consisting of prostate specific antigen, human bone alkaline phosphatase antigen, human chorionic gonadotropin, follicle stimulating hormone, leutenizing hormone, creatine phosphokinase MB isoenzyme, ferritin, carcinoembryonic antigen, CA-549, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antigen, hepatitis B core antibody, hepatitis A virus antibody, hepatitis C virus antibody, the p41 antigen of HIV II, the gp120 antigen of HIV I, the p66 antigen of HIV I, the p41 antigen of HIV I, the p31 antigen of HIV I, the p24 antigen of HIV I, the p17 antigen of HIV I and an antiligand to any one of said aforementioned antigens.
- 32. The series of calibrator solutions of claim 30 wherein the mammalian serum protein is bovine serum albumin.
- 33. The series of calibrator solutions of claims 32 or 29 wherein the dye is selected from the group consisting of Malachite Green, fluorescein, eosin, phenolphthalein, tetramethylrhodamine, and erythrosin.
- $34. \ \,$  The series of calibrator solutions of claim 33 wherein the dye is Malachite Green.
- 35. The series of calibrator solutions of claim 34 wherein the ratio of dye to protein is within the range from about 2.8:1 to about 7:1.
- 36. A method for performing a diagnostic assay for an analyte of interest, the method comprising the steps of: a. providing a series of calibrator solutions spanning a predetermined range of calibrator concentrations, each solution in said series having a predetermined concentration of calibrator therein, said calibrator being the same or substantially the same as the analyte of interest; b. aligning the series of calibrator solutions in an ascending or descending order based upon the concentration of a calibrator material contained therein, each calibrator solution in said series being characterized in that it further contains a visible and non-interfering marker therein in proportion to the concentration of calibrator material contained therein, said marker being a colored dye conjugated to a carrier protein; c. viewing the color of the aligned series of calibrator solutions for non-reversing ascent or descent to assure that the calibrator solutions are in proper alignment for pipetting and/or sampling; whereby a reversal in the ascent or descent of the color in the aligned series of calibrator solutions would indicate misalignment in the assay; and d. performing a diagnostic assay using said series of calibrator solutions.
- 37. A process for confirming the correct dilution of a stock solution containing a calibration or control material ("calibrator") comprising

end deeps of, a, commenting an individual officers and non incorrecting amount of a marker and a predetermined quantity of a calibrator to form a marked stock calibrator solution having a first concentration of said marker and a second concentration of said calibrator, said marker being a dye conjugated to a carrier protein; b. calculating a proportion between the concentration of the marker and the concentration of the calibrator in the marked stock calibrator solution; c. diluting the marked stock calibrator solution or a portion thereof by a predetermined amount to produce a diluted calibrator solution wherein said proportion is substantially maintained, said diluted calibrator solution having a first expected concentration of said marker that is associated with a first expected physical parameter and further having a second expected concentration of said calibrator therein; d. measuring an actual physical parameter of the diluted calibrator solution, the actual physical parameter being proportional to the actual concentration of the marker therein; e. comparing the actual physical parameter or a derivative thereof to the first expected physical parameter or a derivative thereof respectively to confirm that the diluting step was performed correctly.

- $38.\ \mbox{The process of claim}$   $37\ \mbox{wherein the marked stock calibrator solution}$  is an aqueous based solution.
- 39. The process of claim 38 wherein the calibrator is a ligand or an antiligand.
- 40. The process of claim 39 wherein the ratio of dye to carrier protein is within the range from about 1:1 to about 15:1.
- 41. The process of claim 40 wherein the carrier protein is a mammalian serum protein.
- 42. The process of claim 41 wherein the mammalian serum protein is selected from the group consisting of bovine serum albumin, human serum albumin, porcine serum albumin, sheep serum albumin, murine serum albumin, goat serum albumin, and guinea pig serum albumin.
- 43. The process of claims 39 or 42 wherein the calibrator is selected from the group consisting of prostate specific antigen, human bone alkaline phosphatase antigen, human chorionic gonadotropin, follicle stimulating hormone, human leutenizing hormone, creatine phosphokinase MB isoenzyme, ferritin, carcinoembryonic antigen, CA-549, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antigen, hepatitis B core antigen, hepatitis B core antibody, hepatitis A virus antibody, hepatitis C virus antibody, the p41 antigen of HIV II, the gp120 antigen of HIV I, the p66 antigen of HIV I, the p41 antigen of HIV I, the p31 antigen, the p24 antigen of HIV I, the p17 of HIV I, and an antiligand to any one of said aforementioned antigens.
- 44. The process of claim 42 wherein the mammalian serum protein is bovine serum albumin.
- 45. The process of claims 37 or 44 wherein the dye is selected from the group consisting of Malachite Green, fluorescein, eosin, phenolphthalein, and erythrosin.
- 46. The process of claim 44 wherein the dye absorbs light in the visible spectrum.
- $47.\ \,$  The process of claim 46 wherein the dye is a triphenylmethyl type dye.
- 48. The process of claim 46 wherein the dye is Malachite Green.
- 49. A process for confirming that the actual concentration of a calibration or control material ("calibrator") is near its expected concentration in a solution that has been diluted from a stock solution comprising the steps of: a. combining an identifiably effective and non-interfering amount of marker ("the marker") and a predetermined quantity of a calibrator to form a marked stock calibrator solution having a first concentration of the marker and a second concentration of the calibrator, said marker being a dye conjugated to a carrier protein; b. calculating a proportion between the concentration of the marker and the concentration of the calibrator in the marked stock calibrator solution; c. diluting the marked stock calibrator solution or a portion thereof by a predetermined amount to produce a diluted calibrator solution wherein the proportion is substantially maintained, the diluted calibrator having a first expected concentration of the marker that is associated with a first expected physical parameter and further having a second expected concentration of the calibrator therein; d. measuring an actual physical parameter of the diluted calibrator solution, the actual physical parameter being proportional to the actual concentration of the marker therein; e. confirming that the actual concentration of

actual physical parameter, is substantially near its expected concentration.

- 50. The process of claim 49 wherein the stock solution is an aqueous based solution.
- 51. The process of claim 42 wherein the calibrator is a ligand or an antiligand.
- 52. The process of claim 51 wherein the calibrator is selected from the group consisting of prostate specific antigen, human bone alkaline phosphatase antigen, human chorionic gonadotropin, follicle stimulating hormone, human leutenizing hormone, creatine phosphokinase MB isoenzyme, ferritin, carcinoembryonic antigen, hepatitis B surface antigen, hepatitis B surface antigen, hepatitis B core antibody, hepatitis B core antibody, hepatitis C virus antibody, the p41 antigen of HIV II, the gp120 antigen of HIV I, the p66 antigen of HIV I, the p41 antigen of HIV I, the p13 antigen of HIV I, the p24 antigen of HIV I, the p17 antigen of HIV I, and an antiligand to any one of said aforementioned antigens.
- 53. The process of claim 52 wherein the ratio of dye to carrier protein is within the range of from about 1:1 to about 15:1.
- $54.\ \mbox{The process of claim }53\ \mbox{wherein the carrier protein is a mammalian serum protein.}$
- 55. The process of claims 49 or 54 wherein the mammalian serum protein is selected from the group consisting of bovine serum albumin, human serum albumin, porcine serum albumin, sheep serum albumin, murine serum albumin, goat serum albumin and guinea pig serum albumin.
- 56. The process of claim 55 wherein the mammalian serum protein is bovine serum albumin.
- 57. The process of claim 56 wherein the dye absorbs light in the visible spectrum.
- 58. The process of claim 57 wherein the dye is selected from the group consisting of Malachite Green, fluorescein, eosin, tetramethylrhodamine, and erythrosin.
- 59. The process of claim 58 wherein the dye is Malachite Green.
- 60. The process of claim 59 wherein the ratio of Malachite Green to bovine serum albumin is within the range from about 2.8:1 to about 7:1.

L52 ANSWER 22 OF 41 USPATFULL on STN 95:80209 Multi-immunoassay diagnostic system for antigens or antibodies or both

Urnovitz, Howard B., San Francisco, CA, United States Calypte, Inc., Berkeley, CA, United States (U.S. corporation) US 5447837 19950905

APPLICATION: US 1989-307361 19890206 (7)

PRIORITY: CA 1988-573926 19880805 DOCUMENT TYPE: Utility; Granted.

- 1. A kit for detecting the presence of a target human **antibody** to **human immunodeficiency virus** (**HIV**) in a urine sample comprising a) a treatment buffer comprising non-immune sera and about 0.01% to 0.5% (w/v) of a plurality of solid phase particles from about 0.5 microns to about 10 microns in diameter, the plurality of solid phase particles comprising equal volumes of three particle types, each particle type coated with goat, bovine, or horse immunoglobulin antibodies, the non-immune sera comprising 3% bovine serum, 3% goat serum, and 3% horse serum; b) a labelled reagent comprising an enzyme label conjugated to an anti-human immunoglobulin **antibody**; c) a substrate specific for the enzyme label; and d) a reagent **HIV antigen**.
- 2. A buffer comprising non-immune sera and about 0.01% to 0.5% (w/v) of a plurality of solid phase particles from about 0.5 microns to about 10 microns in diameter, the plurality of solid phase particles comprising equal volumes of three particle types, each particle type coated with goat, bovine, or horse immunoglobulin antibodies, the non-immune sera comprising 3% bovine serum, 3% goat serum, and 3% horse serum.
- 3. A method for detecting the presence of a target human **antibody** to **HIV** in a urine sample, said method comprising: a) adding a treatment buffer to the sample, which buffer comprises non-immune sera and 0.01% to 0.5% (w/v) of a plurality of solid phase particles from about 0.5

particles comprising equal volumes of three particle types, each particle type coated with goat, bovine, or horse immunoglobulin antibodies, the non-immune sera comprising 3% bovine serum, 3% goat serum, and 3% horse serum; and b) contacting the sample with a reagent HIV antigen to form an antigen-antibody complex containing the target human antibody and the HIV antigen; c) contacting the antigen-antibody complex with an enzyme labeled anti-human immunoglobulin antibody that specifically binds to the target human antibody; and d) detecting the presence of the bound label as an indication of the presence of any target antibody in the urine sample.

- 4. The method of claim 3 wherein the **HIV antigen** is gp160, gp120 or gp41 glycoprotein, or **p24** protein.
- 5. A method of detecting an HIV antibody in a saliva, urine, or whole or fractionated blood sample from a human subject, said method comprising: a) contacting the sample with a recombinant  ${\tt HIV}$ glycoprotein under conditions such that the glycoprotein specifically binds to any HIV antibody present in the sample to form a complex; b) contacting the complex with an enzyme labeled anti-human immunoglobulin  $\mbox{antibody}$  which specifically binds and labels the complex to form a labeled complex; and c) detecting the presence of enzyme labeled complex and thereby the presence of any HIV antibody in the sample wherein a treatment buffer is added to the sample before, or simultaneous with, contacting the sample with the glycoprotein, said treatment buffer comprising non-immune sera and about 0.01% to 0.5% (w/v) of a plurality of solid phase particles from about 0.5 microns to about 10 microns in diameter, the plurality of solid phase particles comprising equal volumes of three particle types, each particle type coated with goat, bovine, or horse immunoglobulin antibodies, the non-immune sent comprising 3% bovine serum, 3% goat serum, and 3% horse
- 6. A method for detecting in a sample from a human subject the presence of a target human  ${\tt antibody}$  to  ${\tt HIV}$  which specifically binds an  ${\tt HIV}$ vital antigen, said method comprising: a) adding to the sample a treatment buffer comprising non-immune sera and about 0.01% to 0.5% (w/v) of a plurality of solid phase particles from about 0.5 microns to about 10 microns in diameter, the plurality of solid phase particles comprising equal volumes of three particle types, each particle type coated with goat, bovine, or horse immunoglobulin antibodies, the non-immune sent comprising 3% bovine serum, 3% goat serum, and 3% horse serum; b) using a test strip comprising i) a solid support; ii) said HIV viral antigen bound to a first discrete area on the solid support; iii) a non-target human antibody bound to a second discrete area on the solid support as a positive control; and iv) a negative control which will not specifically bind target human antibody or antihuman antibody bound to a third discrete area on the solid support; c) contacting the treated sample with the test strip under conditions such that the  ${\bf HIV}$  viral  ${\bf antigen}$  bound to the test strip specifically binds with any target human antibody present in the treated sample; d) washing the test strip to remove unbound treated sample; e) contacting the resulting test strip with enzyme labeled antihuman antibodies which specifically bind to any target human antibodies bound to, or on, the test strip; f) detecting the presence of enzyme labeled antibodies and thereby the presence of target human antibodies in the sample; and g) verifying the correctness of the detection by determining that the positive control is enzyme labeled and the negative control is not enzyme labeled.
- 7. The method of claim 6 wherein the sample comprises urine, saliva, or whole or fractionated blood.
- 8. A method for detecting in a sample from a human subject the presence of a target human antibody to HIV which specifically bins an HIV viral antigen, said method comprising: a) adding to the sample a treatment buffer comprising non-immune sera and about 0.01% to 0.5~(w/v)of a plurality of solid phase particles from about 0.5 microns to about 10 microns in diameter, the plurality of solid phase particles comprising equal volumes of three particle types each particle type coated with goat, bovine, or horse immunoglobulin antibodies, the non-immune sen comprising 3% bovine serum, 3% goat serum, and 3% horse serum; b) using a test strip comprising: i) wells used as a solid support; ii) said HIV viral antigen bound to discrete areas on the solid support; c) contacting the treated sample with the test strip under conditions such that the HIV viral antigen bound to the test strip specifically binds with any target human antibody present in the treated sample; d) washing the test strip to remove unbound treated sample; e) contacting the resulting test strip with enzyme labeled antihuman antibodies which specifically bind to any target human antibodies bound to, or on, the test strip; and f) detecting the presence of any bound enzyme labeled antibodies using a substrate for

the treated sample.

- 9. The method of claim 8, wherein the **HIV** viral **antigen** is gp160, gp120 or gp41 glycoprotein, or **p24** protein.
- 10. The method of claim 8 wherein the  ${\bf HIV}$  viral  ${\bf antigen}$  is recombinant gp 160.

L52 ANSWER 23 OF 41 USPATFULL on STN

95:7805 Base dissociation assay.

Hyman, Jones M., Durham, NC, United States

Akzo Nobel, N.V., Arnhem, Netherlands (non-U.S. corporation)

US 5384240 19950124

APPLICATION: US 1992-981689 19921125 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

LM What is claimed is:

- 1. A method to enhance the detection of **antigen** in a sample by forming an immunocomplex of the **antigen** with a capture **antibody**, wherein in the sample the **antigen** is complexed with an **antibody** as an immunocomplex, comprising adding a reagent having a basic pH to the sample to adjust the pH to a pH greater than about 8.0, thereby dissociating the immunocomplex and releasing **antigen**; contacting the sample having a pH of greater than about 8.0 with a capture **antibody** bound to a solid substrate, whereby new immunocomplexes are formed; and detecting the presence or absence of the new immunocomplexes, thereby determining the presence or absence of said **antigen**.
- 2. A method according to claim 1, wherein the sample is adjusted to a pH in the range of from about 9.0 to about 14.0.
- 3. A method according to claim 2, wherein the pH range is from about 10.0 to about 12.0.
- 4. A method according to claim 1, wherein the **antigen** is selected from the group consisting of peptides, proteins and haptens.
- 5. A method according to claim 1, where the **antigen** is selected from the group consisting of **Ruman Immunodeficiency Virus** type 1 (HIV-1) **p24 antigen**, **Ruman Immunodeficiency Virus** type 1 (HIV-2) p 24 **antigen**, **antigen** from Human T-Cell Lymphtrophic Virus type 1 (HTLV-I), **antigen** from HTLV-2, and **antigen** from Hepatitis C Virus.
- 6. A method according to claim 1, wherein the antigen is human immunodeficiency virus type 1 p24 antigen.
- 7. A method according to claim 1, wherein the antigen is human immunodeficiency virus type 2 p24 antigen.
- 8. A method according to claim 1, wherein the sample is selected from the group consisting of plasma, serum, urine and cerebral spinal fluid.
- 9. A method according to claim 1, wherein the basic solution is a composition of a salt, a buffer with a pKa at a basic pH, and a surfactant selected from the group consisting of nonionics, anionics, cationics and zwitterionics.
- 10. A method according to claim 9, wherein the salt is NaCl, the buffer is ethanolamine and the surfactant is Triton X-100.
- 11. A method according to claim 10, wherein the NaCl has a concentration of 0 to about 3M, the ethanolamine has a concentration of about 0.01M to about 10M, and the Triton X-100 has a concentration from 0% to about 10%.
- 12. A method according to claim 1, wherein the solid substrate is selected from a group consisting of microtiter plate wells, beads, strips, test tubes, capillary tubes, gold sol, red blood cells and latex particles and wherein dissociating the immunocomplex in the sample and forming immunocomplexes with the capture **antibody** occur concurrently.

L52 ANSWER 24 OF 41 USPATFULL on STN
94:90930 Process for preparing an improved western blot immunoassay.
Chan, Emerson W., Libertyville, IL, United States
Robey, William G., Libertyville, IL, United States
Schulze, Werner, Waukegan, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
US 5356772 19941018
APPLICATION: US 1990-622311 19901205 (7)

CAG TURBUTUS TO BURTIARIE FOR MUTG DA

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A method of detecting the presence of at least one biologically active substance in a sample comprising: (a) purifying at least one antigenic reactive substrate on at least one gel from at least one impure mixture; (b) excising from each said gel at least one segment which contains at least one said purified substrate; (c) selectively transferring each said purified substrate from said segment to a solid support, wherein said purified substrate is effectively attached to said solid support; (d) contacting said purified substrate bearing solid support with a sample suspected of containing at least one immunologically active substance, wherein said active substance and said purified substrate form a binding pair; and (e) detecting the presence of said binding pair on said solid support. Wherein more than one segment containing said purified substrate is separated from the same gel.
- 2. The method of claim 1, wherein said solid support is nitrocellulose.
- 3. A method of detecting the presence of at least one biologically active substance in a sample comprising: (a) purifying at least one antigenic reactive substrate on at least one gel from at least one impure mixture; (b) excising from each said gel at least one segment which contains at least one said purified substrate; (c) selectively transferring each said purified substrate from said segment to a solid support, wherein said purified substrate is effectively attached to said solid support; (d) contacting said purified substrate bearing solid support with a sample suspected of containing at least one immunologically active substance, wherein said active substance and said purified substrate form a binding pair; and (e) detecting the presence of said binding pair on said solid support, wherein more than one segment containing said purified substrate is separated from more than one gel.
- 4. The method of claim 3, wherein said solid support is nitrocellulose.
- 5. A method of detecting the presence of at least one biologically active substance in a sample comprising; (a) purifying at least two antigenic reactive substrates on at least two gels frown at least one impure mixture; (b) excising from each said gel at least one segment which contains at least one said purified substrate; (c) selectively transferring each said purified substrate from said segment to a solid support, wherein said purified substrate is effectively attached to said solid support; (d) contacting said purified substrate bearing solid support with a sample suspected of containing at least one immunologically active substance, wherein said active substance and said purified substrate form a binding pair; and (e) detecting the presence of said binding pair on said solid support.
- 6. The method of claim 5 wherein at least two of said gels comprise one of reducing polyacrylamide and one of non-reducing polyacrylamide.
- 7. The method of claim 5, wherein said solid support is nitrocellulose.
- 8. A method of preparing a solid support capable of detecting the presence of at least one biologically active substance in a sample comprising; (a) purifying at least two antigenic reactive substrates on at least two gels from at least one impure mixture; (b) excising from each said gel at least one segment which contains at least one said purified substrate; (c) selectively transferring each said purified substrate from said segment to a solid support, wherein said purified substrate is effectively attached to said solid support.
- 9. The method of claim 8 wherein said active substance is an antibody.
- 10. The method of claim 8 wherein said reactive substrate is an antigen.
- 11. The method of claim 10 wherein said antigen is selected from the group consisting of HIV and HTLV antigens.
- 12. The method of claim 11 wherein said **HIV** and HTLV antigens are selected from the group consisting of **HIV**-1 gpl20, **HIV**-1 p41, **HIV**-1 **p24**, **HIV**-2 p41 and HTLV-1 p21 antigens.
- 13. The method of claim 8 wherein the amount of said antigenic reactive substrate purified on said gel ranges from 0.5 to 5 micrograms.
- 14. The method of claim 8, wherein said solid support is nitrocellulose.

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The United States of America as Represented by the Secretary of the Navy,
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US 5354654 19941011

APPLICATION: US 1993-92518 19930716 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A lyophilized ligand-receptor complex, prepared by a process comprising: (i) binding a labelled ligand or a labelled receptor to an immobilized receptor or an immobilized ligand, to obtain an immobilized ligand-receptor complex; (ii) washing said immobilized ligand-receptor complex to remove any excess labelled ligand or any excess labelled receptor, to obtain a washed immobilized ligand-receptor complex; and (iii) lyophilizing said washed immobilized ligand-receptor complex, to obtain a lyophilized immobilized ligand-receptor complex, wherein said lyophilizing is carried out .in the presence of a cryoprotectant.
- 2. The lyophilized ligand-receptor complex of claim 1, wherein step (i) is carried out by binding a labelled **antigen** or labelled hapten to an immobilized **antibody** and wherein said lyophilized immobilized ligand-receptor complex is a lyophilized labelled **antigen**-immobilized **antibody** complex or a lyophilized labelled hapten-immobilized **antibody** complex.
- 3. The lyophilized ligand-receptor complex of claim 1, wherein said cryoprotectant is selected from the group consisting of disaccharides, polysaccharides, glycerol, proteins, surfactants, serum, buffers, polyethylene glycol, and dimethyl sulfoxide.
- 4. The lyophilized ligand-receptor complex of claim 1, wherein said immobilized receptor or immobilized ligand is capable of specific binding to an analyte selected from the group consisting of acetylcholine receptor antibody, adenovirus antigens, antibodies against adenovirus, aldosterone, acid phosphatase, alpha-1 fetoprotein, angiotensin converting enzyme, antiDNA antibody, antimitochondrial antibody, beta-2 microglobulin, creatine kinase isoenzymes, lactate dehydrogenase isoenzymes, complement components, chlamydia antigens, antibodies against chlamydia, cortisol, C-peptide, cyclic AMP, erthyropoietin, estradiol, ferritin, folic acid, follicle stimulating hormone, gastrin, glucagon, growth hormone, histocompatibility antigens, blood group antigens A and B, haptoglobin, antibodies against hepatitis A and B, hepatitis A and B antigens, antibodies against herpes, herpes antigens, human chorionic gonadotropin, HIV antigens, antibodies against HIV, antibodies against insulin, insulin, IgA, IgD, IgE, IgG, IgM, H. influenza antigen, antibodies against the H. influenza virus, intrinsic factor antibody, Borrelia burgdorferi antigens, antibodies against Borrelia burgdoferi, luteinizing hormone, metyrapone, myoglobin, neuron-specific-enolase, p24, pancreatic polypeptide, parathyroid hormone, placental lactogen, progesterone, prolactin, prostate specific antigen, rotavirus antigens, antibodies against rotavirus, antibodies against rubella, salmonella, serotonin, somatomedin-C,  $T_3$ ,  $T_4$ , testosterone, thyroglobulin, thyroid stimulating hormone, thyroxine, thyroxine binding globulin, transferrin, tri-iodothyronine, vasoactive intestinal polypeptide, vitamins  $B_{6}\ \text{and}\ B_{12}$ , staphylococcus antigens, antibodies against staphylococcus, enterotoxins, ricin, endotoxin, botulism toxin, venoms, amphetamine, methamphetamine, phenobarbital, cocaine, methadone, methaqualone, opiates (morphine, heroin), tetrahydrocannabinol (THC), phencyclidine (PCP), lysergic acid diethylamide (LSD), annabolic steroids, phenyl-butazone, amikacin, azidothymidine, benzodiazepines (diazepam and chlordiazepoxide), carbamazine, chloramphenicol, cyclosporine, digitoxin, digoxin, ethosuximide, gentamicin, imipramine, lidocaine, phenytoin, primidone, procainamide, propoxyphene, propranolol, quinidine, theophylline, tobramycin, valproic acid, trinitrotoluene, cyclonite, pentaerythritol tetranitrate, picric acid, nitroglycerin, herbicides, insecticides, polychlorinated biphenyls, polyaromatic hydrocarbons, heavy metals, glucose, F1 antigen of Y pestis, lethal factor or PA antigen from B. anthracis, and mycotoxins.
- 5. A process for preparing a lyophilized ligand-receptor complex, comprising: (i) binding a labelled ligand or a labelled receptor to an immobilized receptor or an immobilized ligand, to obtain an immobilized ligand-receptor complex; (ii) washing said immobilized ligand-receptor complex to remove any excess labelled ligand or any excess labelled receptor, to obtain a washed immobilized ligand-receptor complex; and (iii) lyophilizing said washed immobilized ligand-receptor complex, to obtain a lyophilized immobilized ligand-receptor complex, wherein said lyophilizing is carried out in the presence of a cryoprotectant.
- 6. The process of claim 5, wherein step (i) is carried out by binding a

wherein said lyophilized immobilized ligand-receptor complex is a lyophilized labelled antigen-immobilized antibody complex or a lyophilized labelled hapten-immobilized antibody complex.

- 7. The process of claim 5, wherein said cryoprotectant is selected from the group consisting of disaccharides, polysaccharides, glycerol, proteins, surfactants, serum, buffers, polyethylene glycol, and dimethyl sulfoxide.
- 8. The process of claim 5, wherein said immobilized receptor or immobilized ligand is capable of specific binding to an analyte selected from the group consisting of acetylcholine receptor antibody, adenovirus antigens, antibodies against adenovirus, aldosterone, acid phosphatase, alpha-1 fetoprotein, angiotensin converting enzyme, antiDNA antibody, antimitochondrial antibody, beta-2 microglobulin, creatine kinase isoenzymes, lactate dehydrogenase isoenzymes, complement components, chlamydia antigens, antibodies against chlamydia, cortisol, C-peptide, cyclic AMP, erthyropoietin, estradiol, ferritin, folic acid, follicle stimulating hormone, gastrin, glucagon, growth hormone, histocompatibility antigens, blood group antigens A and B, haptoglobin, antibodies against hepatitis A and B, hepatitis A and B antigens, antibodies against herpes, herpes antigens, human chorionic gonadotropin, HIV antigens, antibodies against HIV, antibodies against insulin, insulin, IgA, IgD, IgE, IgG, IgM, H. influenza antigen, antibodies against the H. influenza virus, intrinsic factor antibody, Borrelia burgdorferi antigens, antibodies against Borrelia burgdoferi, luteinizing hormone, metyrapone, myoglobin, neuron-specific-enolase, p24, pancreatic polypeptide, parathyroid hormone, placental lactogen, progesterone, prolactin, prostate specific antigen, rotavirus antigens, antibodies against rotavirus, antibodies against rubella, salmonella, serotonin, somatomedin-C, T3, T4, testosterone, thyroglobulin, thyroid stimulating hormone, thyroxine, thyroxine binding globulin, transferrin, tri-iodothyronine, vasoactive intestinal polypeptide, vitamins B6 and B12, staphylococcus antigens, antibodies against staphylococcus, enterotoxins, ricin, endotoxin, botulism toxin, venoms, amphetamine, methamphetamine, phenobarbital, cocaine, methadone, methaqualone, opiates (morphine, heroin), tetrahydrocannabinol (THC), phencyclidine (PCP), lysergic acid diethylamide (LSD), annabolic steroids, phenyl-butazone, amikacin, azidothymidine, benzodiazepines (diazepam and chlordiazepoxide), carbamazine, chloramphenicol, cyclosporine, digitoxin, digoxin, ethosuximide, gentamicin, imipramine, lidocaine, phenytoin, primidone, procainamide, propoxyphene, propranolol, quinidine, theophylline, tobramycin, valproic acid, trinitrotoluene, cyclonite, pentaerythritol tetranitrate, picric acid, nitroglycerin, herbicides, insecticides, polychlorinated biphenyls, polyaromatic hydrocarbons, heavy metals, glucose, F1 antigen of Y pestis, lethal factor or PA-antigen from B. anthracis, and mycotoxins.
- 9. A lyophilized, dry reagent, comprising: (a) a labeled ligand or labeled receptor bound to (b) a complementary receptor or a complementary ligand, wherein said complementary receptor or complementary ligand is immobilized on a solid support, wherein said lyophilized, dry reagent is prepared by lyophilizing in the presence of a cryoprotectant.
- 10. The dry reagent of claim 9, comprising a labelled **antigen** or labelled hapten bound to a complementary **antibody**, wherein said complementary **antibody** is immobilized on a solid support.
- 11. The lyophilized, dry reagent of claim 9, wherein said immobilized receptor or immobilized ligand is capable of specific binding to an analyte selected from the group consisting of acetylcholine receptor antibody, adenovirus antigens, antibodies against adenovirus, aldosterone, acid phosphatase, alpha-1 fetoprotein, angiotensin converting enzyme, antiDNA antibody, antimitochondrial antibody, beta-2 microglobulin, creatine kinase isoenzymes, lactate dehydrogenase isoenzymes, complement components, chlamydia antigens, antibodies against chlamydia, cortisol, C-peptide, cyclic AMP, erthyropoietin, estradiol, ferritin, folic acid, follicle stimulating hormone, gastrin, glucagon, growth hormone, histocompatibility antigens, blood group antigens A and B, haptoglobin, antibodies against hepatitis A and B, hepatitis A and B antigens, antibodies against herpes, herpes antigens, human chorionic gonadotropin, HIV antigens, antibodies against HIV, antibodies against insulin, insulin, IgA, IgD, IgE, IgG, IgM, H. influenza antigen, antibodies against the H. influenza virus, intrinsic factor antibody, Borrelia burgdorferi antigens, antibodies against Borrelia burgdoferi, luteinizing hormone, metyrapone, myoglobin, neuron-specific-enolase, p24, pancreatic polypeptide, parathyroid hormone, placental lactogen, progesterone, prolactin, prostate specific antigen, rotavirus antigens, antibodies against rotavirus, antibodies against rubella, salmonella, serotonin, somatomedin-C, T3, T4,

conconcoror, chilogropheris, chilora nermaracris normone, chilonric, thyroxine binding globulin, transferrin, tri-iodothyronine, vasoactive intestinal polypeptide, vitamins B6 and B12, staphylococcus antigens, antibodies against staphylococcus, enterotoxins, ricin, endotoxin, botulism toxin, venoms, amphetamine, methamphetamine, phenobarbital, cocaine, methadone, methaqualone, opiates (morphine, heroin), tetrahydrocannabinol (THC), phencyclidine (PCP), lysergic acid diethylamide (LSD), annabolic steroids, phenyl-butazone, amikacin, azidothymidine, benzodiazepines (diazepam and chlordiazepoxide), carbamazine, chloramphenicol, cyclosporine, digitoxin, digoxin, ethosuximide, gentamicin, imipramine, lidocaine, phenytoin, primidone, procainamide, propoxyphene, propranolol, quinidine, theophylline, tobramycin, valproic acid, trinitrotoluene, cyclonite, pentaerythritol tetranitrate, picric acid, nitroglycerin, herbicides, insecticides, polychlorinated biphenyls, polyaromatic hydrocarbons, heavy metals, glucose, Fl antigen of Y pestis, lethal factor or PA antigen from B. anthracis, and mycotoxins.

- 12. A displacement assay for detecting an analyte in a sample, comprising: (a) contacting a sample which may contain said analyte with an immobilized ligand-receptor complex prepared by a process comprising: (i) binding a labelled ligand or a labelled receptor to an immobilized receptor or an immobilized ligand, to obtain an immobilized ligand-receptor complex; (ii) washing said immobilized ligand-receptor complex to remove any excess labelled ligand or any excess labelled receptor, to obtain a washed immobilized ligand-receptor complex; (iii) lyophilizing said washed immobilized ligand-receptor complex, to obtain a lyophilized immobilized ligand-receptor complex, wherein said lyophilizing is carried out in the presence of a cryoprotectant; and (iv) rehydrating said lyophilized immobilized ligand-receptor complex; and (b) measuring (1) the amount of labelled ligand or labelled receptor displaced from said immobilized receptor or said immobilized ligand, or (2) the amount of labelled ligand or labelled receptor which remains bound to said immobilized receptor or said immobilized ligand.
- 13. The displacement assay of claim 12, wherein step (i) is carried out by binding a labelled **antigen** or labelled hapten to an immobilized **antibody** and wherein said lyophilized immobilized ligand-receptor complex is a lyophilized labelled **antigen**-immobilized **antibody** complex or a lyophilized labelled hapten-immobilized **antibody** complex.
- 14. The displacement assay claim 12, wherein said cryoprotectant is selected from the group consisting of disaccharides, polysaccharides, glycerol, proteins, surfactants, serum, buffers, polyethylene glycol, and dimethyl sulfoxide.
- 15. The displacement assay of claim 12, wherein said immobilized receptor or immobilized ligand is capable of specific binding to an analyte selected from the group consisting of acetylcholine receptor antibody, adenovirus antigens, antibodies against adenovirus, aldosterone, acid phosphatase, alpha-1 fetoprotein, angiotensin converting enzyme, antiDNA antibody, antimitochondrial antibody, beta-2 microglobulin, creatine kinase isoenzymes, lactate dehydrogenase isoenzymes, complement components, chlamydia antigens, antibodies against chlamydia, cortisol, C-peptide, cyclic AMP, erthyropoietin, estradiol, ferritin, folic acid, follicle stimulating hormone, gastrin, glucagon, growth hormone, histocompatibility antigens, blood group antigens A and B, haptoglobin, antibodies against hepatitis A and B, hepatitis A and B antigens, antibodies against herpes, herpes antigens, human chorionic qonadotropin, HIV antigens, antibodies against HIV, antibodies against insulin, insulin, IgA, IgD, IgE, IgG, IgM, H. influenza antigen, antibodies against the H. influenza virus, intrinsic factor antibody, Borrelia burgdorferi antigens, antibodies against Borrelia burgdoferi, luteinizing hormone, metyrapone, myoqlobin, neuron-specific-enolase, p24, pancreatic polypeptide, parathyroid hormone, placental lactogen, progesterone, prolactin, prostate specific antigen, rotavirus antigens, antibodies against rotavirus, antibodies against rubella, salmonella, serotonin, somatomedin-C, T3, T4, testosterone, thyroglobulin, thyroid stimulating hormone, thyroxine, thyroxine binding globulin, transferrin, tri-iodothyronine, vasoactive intestinal polypeptide, vitamins  $B_6$  and  $B_{12}$ , staphylococcus antigens, antibodies against staphylococcus, enterotoxins, ricin, endotoxin, botulism toxin, venoms, amphetamine, methamphetamine, phenobarbital, cocaine, methadone, methaqualone, opiates (morphine, heroin), tetrahydrocannabinol (THC), phencyclidine (PCP), lysergic acid diethylamide (LSD), annabolic steroids, phenyl-butazone, amikacin, azidothymidine, benzodiazepines (diazepam and chlordiazepoxide ), carbamazine, chloramphenicol, cyclosporine, digitoxin, digoxin, ethosuximide, gentamicin, imipramine, lidocaine, phenytoin, primidone, procainamide, propoxyphene, propranolol, quinidine, theophylline, tobramycin, valproic acid, trinitrotoluene, cyclonite, pentaerythritol tetranitrate, picric acid, nitroglycerin, herbicides, insecticides, polychlorinated biphenyls, polyaromatic hydrocarbons, heavy metals,

anthracis, and mycotoxins.

- 16. The displacement assay of claim 12, wherein said contacting comprises flowing said sample past said immobilized ligand-receptor complex at a flow rate allowing said analyte to displace said labelled ligand or said labelled receptor from said ligand-receptor complex under nonequilibrium conditions.
- 17. The displacement assay of claim 16, wherein said flowing of said sample past said immobilized ligand-receptor complex is carried out in a column.
- 18. The displacement assay of claim 16, wherein said flowing of said sample past said ligand-receptor complex is carried out at a flow rate between 0.1 and 2.0 milliliters per minute.
- 19. The displacement assay of claim 16, wherein said flowing of said sample past said ligand-receptor complex is carried out at a flow rate between 0.3 and 0.8 milliliters per minute.
- 20. A kit, comprising a lyophilized, dry reagent comprising: (a) a labeled ligand or labeled receptor bound to (b) a complementary receptor or a complementary ligand, wherein said complementary receptor or complementary ligand is immobilized on a solid supports, wherein said lyophilized, dry reagent is prepared by lyophilizing in the presence of a cryoprotectant.
- 21. The kit of claim 20, comprising a labelled **antigen** or labelled hapten bound to a complementary **antibody**, wherein said complementary **antibody** is immobilized on a solid support.
- 22. The kit of claim 20, wherein said complementary receptor or complementary ligand is capable of specific binding to an analyte selected from the group consisting of acetylcholine receptor antibody, adenovirus antigens, antibodies against adenovirus, aldosterone, acid phosphatase, alpha-1 fetoprotein, angiotensin converting enzyme, antiDNA antibody, antimitochondrial antibody, beta-2 microglobulin, creatine kinase isoenzymes, lactate dehydrogenase isoenzymes, complement components, chlamydia antigens, antibodies against chlamydia, cortisol, C-peptide, cyclic AMP, erthyropoietin, estradiol, ferritin, folic acid, follicle stimulating hormone, gastrin, glucagon, growth hormone, histocompatibility antigens, blood group antigens A and B, haptoglobin, antibodies against hepatitis A and B, hepatitis A and B antigens, antibodies against herpes, herpes antigens, human chorionic qonadotropin, HIV antigens, antibodies against HIV, antibodies against insulin, insulin, IgA, IgD, IgE, IgG, IgM, H. influenza antigen, antibodies against the H. influenza virus, intrinsic factor antibody, Borrelia burgdorferi antigens, antibodies against Borrelia burgdoferi, luteinizing hormone, metyrapone, myoglobin, neuron-specific-enolase, p24, pancreatic polypeptide, parathyroid hormone, placental lactogen, progesterone, prolactin, prostate specific antigen, rotavirus antigens, antibodies against rotavirus, antibodies against rubella, salmonella, serotonin, somatomedin-C, T3, T4, testosterone, thyroglobulin, thyroid stimulating hormone, thyroxine, thyroxine binding globulin, transferrin, tri-iodothyronine, vasoactive intestinal polypeptide, vitamins  $B_6$  and  $B_{12}$ , staphylococcus antigens, antibodies against staphylococcus, enterotoxins, ricin, endotoxin, botulism toxin, venoms, amphetamine, methamphetamine, phenobarbital, cocaine, methadone, methaqualone, opiates (morphine, heroin), tetrahydrocannabinol (THC), phencyclidine (PCP), lysergic acid diethylamide (LSD), annabolic steroids, phenyl-butazone, amikacin, azidothymidine, benzodiazepines (diazepam and chlordiazepoxide), carbamazine, chloramphenicol, cyclosporine, digitoxin, digoxin, ethosuximide, gentamicin, imipramine, lidocaine, phenytoin, primidone, procainamide, propoxyphene, propranolol, quinidine, theophylline, tobramycin, valproic acid, trinitrotoluene, cyclonite, pentaerythritol tetranitrate, picric acid, nitroglycerin, herbicides, insecticides, polychlorinated biphenyls, polyaromatic hydrocarbons, heavy metals, glucose, F1 antigen of Y pestis, lethal factor or PA antigen from B. anthracis, and mycotoxins.

## L52 ANSWER 26 OF 41 USPATFULL on STN

93:87245 Immunoassays using antigens produced in heterologous organisms.
Mimms, Larry T., Lake Villa, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
US 5254458 19931019

APPLICATION: US 1992-922354 19920729 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. In the method of performing a sandwich immunoassay for detecting

antigen specific to the antibody to be detected is immobilized on a solid phase, wherein the antibody to be detected in the test sample binds to the first antigen thereby becoming immobilized, wherein said immobilized antibody further binds a second antigen bearing a label, and wherein the first antigen and the second antigen are derived from a homologous source; the improvement comprising deriving the second antigen from a source that is heterologous to the source of the first antigen.

- 2. A method for detecting an **antigen** specific **antibody** in a test sample comprising the steps of: (a) immobilizing a first recombinant derived **antigen** specific to the **antibody** to be detected on a solid phase; (b) contacting the solid phase produced in step (a) with an aqueous phase test sample containing or suspected of containing the **antigen** specific **antibody**; (c) contacting the solid phase produced in step (b) with an aqueous phase containing a second recombinant derived **antigen** having a label affixed thereto, the second recombinant derived **antigen** being derived from a source that is heterologous to the source of said first recombinant derived **antigen**; (d) separating the aqueous phase from the solid phase; (e) measuring the presence of the label on the solid phase or in the liquid phase to detect and/or titer the presence of **antibody** in the test sample.
- 3. The method of claim 2 wherein the label is an enzyme or radioisotope.
- 4. The method of claim 2 wherein both the first and second recombinant derived antigens simultaneously possess at least one antigenic determinant in common, said antigenic determinant being a member of the group consisting of the **p24 antigen** of HTLV III, the p41 **antigen** of HTLV III, the gp120 **antigen** of HTLV III, HBsAg, HBcAg, With the proviso that the first and second recombinant derived antigens have sufficient antigenic determinants in common to permit cross-linking by **antigen** specific **antibody** in the test sample.
- 5. The method of claim 2 wherein steps (b) and (c) are performed simultaneously.
- 6. The immunoassay of claim 2 wherein the solid phase is a polystyrene bead.
- 7. A method for detecting antibody to the p41 antigen of HTLV III which may be present in a human serum sample, comprising the steps of: a. coating a polystyrene bead with purified p41 antigen from yeast; b. adding the human serum sample to the coated bead; c. incubating for about 2 hours at approximately 40° C.; d. washing the bead with deionized water; e. adding to the bead a purified p41 antigen of HTLV III labeled with a detectable label which antigen simultaneously possesses at least one antigenic determinant in common with said antigen of step (a) wherein said antigen is derived from an organism heterologous from that used to produce the p41 antigen of HTLV III coated on the bead; said antigen having sufficient antigenic determinants in common with the antigen of step (a), thereby permitting cross-linking by an **antibody** to p41 in the human serum sample; f. incubating for about 1 hour at approximately 40° C.; g. washing the bead with deionized water; h. separating unreacted reagents from the bead; and i. measuring the presence of the labeled p41 antigen to HTLV III on the bead.
- 8. The method of claim 7 wherein the p41 **antigen** of step (a) is produced in yeast, and the labeled p41 **antigen** of step (e) is produced in E. coli.
- 9. The method of claim 7 wherein the p41 antigen of step (e) is produced in mouse cells.
- 10. The method of claim 7 wherein the detectable label is 125 I.
- 11. The method of claim 7 wherein the detectable label is horseradish peroxidase.
- 12. The method of claim 7 wherein step (c) comprises incubating for 2 hours at 40° C., and step (f) comprises incubating for 1 hour at 40° C.
- 13. A method for detecting an **antigen** specific **antibody** which may be present in a test sample comprising the steps of: (a) immobilizing a first **antigen** specific to the **antibody** to be detected on a solid phase; (b) contacting the solid phase produced in step (a) with an aqueous phase test sample containing or suspected of containing the **antigen** specific **antibody**; (c) contacting the solid phase produced in step (b) with an aqueous phase containing a second **antigen** having a label affixed thereto, said second **antigen** being derived from a source

ends to necessaged to one bound of bard first michael, (a) separating the aqueous phase form the solid phase; (e) measuring the presence of the label on the solid phase or in the liquid phase to detect and/or titer the presence of antibody in the test sample.

- 14. A method for detecting an antigen specific antibody in a test sample comprising: (a) contacting an aqueous phase test sample containing or suspected of containing the antigen specific antibody with a solid phase upon which a first recombinant derived antigen specific to the antibody has been immobilized; (b) contacting said solid phase of step (a) with an aqueous phase containing a second recombinant derived antigen having a label affixed thereto, said second derived antigen being derived from a source that is heterologous to the source of said first recombinant derived antigen; (c) separating the aqueous phase from the solid phase; and (d) measuring the presence of the label on the solid phase or in the liquid phase to detect and/or tier the presence of antibody in the test sample.
- 15. The method of claim 14 wherein both the first and second recombinant derived antigens simultaneously possess at least one antigenic determinant in common, said antigenic determinant being a member of the group consisting of the p24 antigen of HTLV III, the p41 antigen of HTLV III, the gp120 antigen of HTLV III, HBsAg, HBcAg and HBeAg, with the proviso that the first and second recombinant derived antigens have sufficient antigenic determinants in common to permit cross-linking by antigen specific antibody in the test sample.
- 16. The method of claim 14 wherein step (a) and step (b) are performed simultaneously.
- 17. The method of claim 14 wherein said label is selected from the group consisting of an enzyme, a radioisotope, and a fluorescent marker.
- 18. The method of claim 14 wherein the solid phase is selected from the group consisting of a microparticle, a bead, a test tube, modified cellulose material, glass fibrous matrices and plastic fibrous matrices.
- 19. A method for detecting an antigen specific antibody in a test sample comprising: (a) contacting an aqueous phase test sample containing or suspected of containing the antigen specific antibody with a solid phase upon which a first antigen specific to the antibody has been immobilized; (b) contacting said solid phase of step (a) with an aqueous phase containing a second antigen having a label affixed thereto, said second derived antigen being derived from a source that is heterologous to the source of said first derived antigen; (c) separating the aqueous phase from the solid phase; and (d) measuring the presence of the label on the solid phase or in the liquid phase to detect and/or titer the presence of antibody in the test sample.
- 20. The method of claim 19 wherein both the first and second antigens simultaneously possess at least one antigenic determinant in common, said antigenic determinant being a member of the group consisting of the p24 antigen of HTLV III, the p41 antigen of HTLV III, the gp120 antigen of HTLV III, HBsAg, HBcAg and HBeAg, with the proviso that the first and second antigens have sufficient antigenic determinants in common to permit cross-linking by antigen specific antibody in the test sample.
- 21. The method of claim 19 wherein step (a) and step (b) are performed simultaneously.
- 22. The method of claim 19 wherein said label is selected from the group consisting of an enzyme, a radioisotope, and a fluorescent marker.
- 23. The method of claim 19 wherein the solid phase is selected from the group consisting of a microparticle, a bead, a test tube, modified cellulose material, glass fibrous matrices and plastic fibrous matrices.

L52 ANSWER 27 OF 41 USPATFULL on STN 93:48385 Monoclonal antibodies to feline-T-lymphotropic lentivirus. O'Connor, Thomas P., Westbrook, ME, United States Tonelli, Quentin J., Portland, ME, United States Idexx Laboratories Incorporated, Westbrook, ME, United States (U.S. corporation) US 5219725 19930615 APPLICATION: US 1989-293906 19890105 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

What is claimed is:

1. A monoclonal antibody specific for an epitope of the feline immunodeficiency virus, FIV encoded antigen 10.

- 2. A monoclonal **antibody** specific for an epitope of the FIV-encoded **antigen** pll0.
- 3. A monoclonal **antibody** specific for an epitope of the FIV-encoded **antigen** qp130.
- 4. A composition comprising at least two monoclonal antibodies, each **antibody** being specific for a different epitope of an FIV-encoded antigenic protein, said antigenic protein being chosen from the group consisting of p10, p15, **p26**, p47, p110, gp40, gp130.
- 5. A method for detection of an epitope of an FIV-encoded antigenic protein in a sample, said antigenic protein being chosen from the group consisting of p10, p15, p26, p110, gp40, gp130, said method comprising the steps of: a) providing a monoclonal antibody specific for said epitope; b) contacting said antibody with said sample under conditions in which said antibody forms a complex with said epitope; and c) detecting said complex, wherein the presence of said complex indicates the presence of said epitope in said sample.
- L52 ANSWER 28 OF 41 USPATFULL on STN
- 92:104887 Mouse monoclonal antibodies to  ${f hiv}$ -1p24 and their use in diagnostic tests.

Mehta, Smriti U., Libertyville, IL, United States Hunt, Jeffrey C., Lindenhurst, IL, United States Devare, Sushil G., Northbrook, IL, United States Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation) US 5173399 19921222

APPLICATION: US 1988-204798 19880610 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. An immunoassay for the detection of HIV-I p24 antigen in a test sample comprising forming an antibody/antigen complex wherein the antibody portion of said complex comprises a mixture of murine monoclonal antibodies, at least one monoclonal antibody of said mixture being capable of specifically binding to an epitope on HIV-I p24 to which epitope human anti-HIV-I p24 lgG does not competitively bind, and at least one other monoclonal antibody of said mixture being capable of binding to a different epitope of HIV-I p24 to which different epitope human anti-HIV-I p24 lgG competitively binds, and detecting the presence or amount in picogram sensitivity of the antibody/antigen complex formed.
- 2. The immunoassay of claim 1 wherein the presence or amount of the antibody/antigen complex formed is determined by incubating said complex with a labelled, anti-species antibody specific for said monoclonal antibodies.
- 3. The immunoassay of claim 2 wherein said label comprises a radioisotope, enzyme, fluorescent compound, chemiluminescent compound, or member of a specific binding pair.
- 4. The immunoassay of claim 1 wherein the **antibody** which binds to the epitope on **HIV-1 p24** to which epitope human anti-**HIV-1 p24** IgG does not competitively bind is monoclonal **antibody** 31-42-19 and the **antibody** which binds to the different epitope to which different epitope human anti-**HIV-1 p24** IgG competitively binds is monoclonal **antibody** 31-90-25.
- 5. The immunoassay of claim 4 wherein said monoclonal antibodies 31-42-19 and 31-90-25 are in solution.
- 6. The immunoassay of claim 4 wherein said monoclonal antibodies 31-42-19 and 31-90-25 are coated on a solid support.
- 7. The immunoassay of claim 5 wherein said **antibody** portion of said complex further comprises human anti-**HIV-**I IgG coated on a solid support.
- 8. The immunoassay of claim 6 wherein said **antibody** portion of said complex further comprises an anti-HIV-I **antibody** or a fragment thereof.
- 9. The immunoassay of claim 8 wherein said antibody portion of said complex further comprises anti-HIV-I  $F(ab')_2$ .
- 10. The immunoassay of claim 9 wherein said **antibody** portion of said complex further comprises anti-**HIV-I p24** F(ab')<sub>2</sub>.
- 11. A diagnostic reagent for detection of HIV-1 p24 antigen or HIV-2 p24 antigen comprising a monoclonal antibody which

resoured prima an air abreadha air mer e bee an intair abreadh iomhair anti-HIV-1 p24 IgG does not competitively bind and which monoclonal antibody also specifically binds to HIV-2 p24.

- 12. An immunoassay for the detection of  ${\bf HIV}\text{--}1~{\bf p24}$  antigen in a human test sample comprising: a. contacting a human test sample with a solid support coated with human anti- ${\tt HIV-1}$  IgG for a time and under conditions sufficient to form antibody/antigen complexes; b. contacting said complexes with a murine monoclonal antibody mixture comprising monoclonal antibodies 31-42-19 secreted by ATCC HB 9726 and 31-90-25 secreted by ATCC HB 9725 for a time and under conditions sufficient to form antibody/antigen/antibody complexes; c. contacting said antibody/antigen/antibody complexes with an anti-mouse antibody or fragment thereof conjugated to a detectable label capable of generating a measurable signal; d. measuring the signal generated to determine the presence of  ${\tt HIV-l}$   ${\tt p24}$  in picogram sensitivity in the test sample.
- 13. The immunoassay of claim 12 wherein said solid support is simultaneously contacted with said human test sample and said mouse monoclonal antibody mixture.
- 14. An immunoassay for detection of the presence or amount of HIV-2 p24 antigen in a human test sample, comprising forming an antibody/antigen complex wherein the antibody portion of said complex comprises a monoclonal antibody capable of specifically binding to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind and which monoclonal antibody also specifically binds to  ${\tt HIV-2~p24}$  , and detecting the presence or amount of the antibody/antigen complex formed.
- 15. A diagnostic kit for the detection of HIV-1 p24 antigen comprising: a container containing a mixture of at least two murine monoclonal antibodies wherein at least one monoclonal antibody of said mixture specifically binds to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind and wherein at least one other monoclonal antibody of said mixture specifically binds to a different epitope of HIV-1 p24 to which different epitope human anti-HIV-1 p24 IgG competitively binds.
- 16. The diagnostic kit of claim 15 wherein said murine monoclonal antibody which specifically binds to an epitope on HIV-1 p24 to which epitope human anti-HIV-1 p24 IgG does not competitively bind is designated as monoclonal **antibody** 31-42-19 secreted by the hybridoma cell line ATCC 9726 and wherein said monoclonal antibody which is capable of binding to a different epitope of HIV-1 p24 to which different epitope human anti-HIV-1 p24 IgG competitively binds is designated as the 31-90-25 monoclonal antibody secreted by the hybridoma cell line ATCC HB 9725.
- 17. The immunoassay of claim 12 wherein said solid support is selected from the group consisting of wells of reaction trays, test tubes, polystyrene beads, strips, membranes and microparticles.
- 18. The immunoassay of claim 12 wherein said label is selected from the group consisting of enzymes, radioisotopes, fluorescent compounds and chemiluminescent compounds.
- 19. The immunoassay of claim 18 wherein said enzymatic label is horseradish peroxidase.
- 20. The immunoassay of claim 12, 18 or 19 further comprising a hapten and labelled anti-hapten system wherein the hapten is conjugated to the labeled murine monoclonal antibody.
- 21. The diagnostic reagent of claim 20 wherein said monoclonal antibody is the monoclonal antibody secreted by the hybridoma cell line A.T.C.C. HB 9726.

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L52 ANSWER 29 OF 41 USPATFULL on STN
92:94983 Monoclonal antibody for detecting HTLV-I, HTLV-II and STLV-I viruses.
    Hofheinz, David E., Davie, FL, United States
    Toedter, Gary P., Ft. Lauderdale, FL, United States
    Charie, Lori A., Hollywood, FL, United States
    Pearlman, Samuel R., Davie, FL, United States
Coulter Corporation, Hialeah, FL, United States (U.S. corporation)
    US 5164293 19921117
    APPLICATION: US 1990-587725 19900925 (7)
    DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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CLM

What is claimed is:

1. A hybridoma cell line which produces a monoclonal antibody which

epochizoni, binas co an opisopo or an america commun co naman i colymphotropic viruses type I and II, which cell line is on deposit with the American Type Culture Collection and assigned A.T.C.C. Deposit No. HB 10562.

- 2. The monoclonal antibody produced from the cell line having a A.T.C.C. Deposit No. HB 10562.
- 3. A monoclonal antibody which specifically binds to an antigenic determinant of the HTLV-I, HTLV-II and STLV-I p24, p33 and p53 core antigens, and does not bind to the p19 core antigen, said monoclonal antibody binding the same epitope as the monoclonal antibody produced by the hybridome cell line identified by A.T.C.C. Deposit No. HB 10562.
- 4. An immunoassay for detecting HTLV-I and HTLV-II antigens in biological samples and tissue culture media, said assay comprising: (a) introducing a predetermined volume of test sample into contact with a solid surface to which is bound a known quantity of a monoclonal antibody that specifically binds to a common epitope of HTLV-I and HTLV-II p24, p33 and p53 core antigens and does not bind to the p19 core antigen, said monoclonal antibody binding the same epitope as the monoclonal **antibody** produced by the hybridoma cell line identified as A.T.C.C. Deposit No. HB 10562; (b) incubating said test sample in contact with said surface to form resultant antigen-antibody complexes; (c) incubating the resultant complexes and subjecting same to a labelled human polyclonal anti-HTLV antibody which is capable of yielding a quantitatively measurable signal correlated to the signal for a normal negative test sample; and (d) determining the presence and amount of antigen in the sample by an analytical means utilizing said label.
- 5. The immunoassay of claim 4 wherein simian T-leukemia virus type I is detected.
- 6. A hybridoma cell line which produces a monoclonal antibody which specifically binds to a common antigenic determinant of HTLV-I, HTLV-II and STLV-I p24,p33 and p53 core antigens, and does not bind to the p19 core antigen, said cell line producing a monoclonal antibody which binds to the same epitope as does the monoclonal antibody produced by A.T.C.C. Deposit No. HB 10562.

## L52 ANSWER 30 OF 41 USPATFULL on STN

92:63788 Human Immunodeficiency Virus (HIV) associated with Acquired Immunual Deficiency Syndrome (AIDS), a diagnostic method for aids and pre-aids, and a kit therefor. Montagnier, Luc, Le Plessis Robinson, France Chermann, Jean-Claude, Elancourt, France Barre-Sinoussi, Francoise, Issy Les Moulineaux, France Brun-Vezinet, Francoise, Paris, France Rouzioux, Christine, Paris, France Rozenbaum, Willy, Paris, France Dauguet, Charles, Paris, France Gruest, Jacqueline, L'Hay Les Roses, France Nugeyre, Marie-Therese, Paris, France Rey, Francoise, Paris, France Axler-Blin, Claudine, Paris, France Chamaret, Solange, Paris, France Gallo, Robert C., Bethesda, MD, United States Popovic, Mikulas, Bethesda, MD, United States Sarngadharan, Mangalasseril G., Vienna, VA, United States Institut Pasteur, Paris Cedex, France (non-U.S. corporation) The United States of America as represented by the Secretary of The Department of Health and Human Services, Washington, DC, United States (U.S. government) US 5135864 19920804

APPLICATION: US 1987-117937 19871105 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- 1. A human retrovirus, wherein the retrovirus is Human Immunodeficiency Virus (HIV) in a purified form.
- 2. An in vitro culture of Human Immunodeficiency Virus (HIV) essentially free of other human retroviruses.
- 3. An isolate of a retrovirus, which is Human Immunodeficiency Virus (HIV), wherein the isolate comprises one or a mixture of antigens of said retrovirus, wherein said antigens comprise protein, glycoprotein, or a mixture thereof of said retrovirus, and said antigens are immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).

- 4. A suspension of a retrovirus, which is **Ruman Immunodeficiency Virus** (**HIV**), in a buffer therefor, wherein the suspension comprises a mixtue of antigens of said retrovirus, wherein said antigens comprise protein, glycoprotein, or a mixture thereof of said retrovirus, and said antigens are immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 5. A mixture of antigens of **Human Immunodeficiency Virus** (**HIV**), wherein said antigens comprise protein, glycoprotein, or a mixture thereof of **HIV**, and wherein said antigens are in a purified form and are capable of being immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 6. An  $antigen\ \, of\ \, said\ \, mixture\ \, as\ \, claimed\ \, in\ \, claim\ \, 5,\ \, wherein\ \, said\ \, protein\ \, is\ \, p25$  protein of HIV.
- 7. A mixture of structural proteins of **Human Immunodeficiency Virus** (**HIV**), wherein said proteins comprise protein, glycoprotein, or a mixture thereof of **HIV**, and wherein said proteins are in a purified form.
- 8. A structural protein of said mixture as claimed in claim 7, wherein said protein is envelope protein of **HIV**.
- 9. A structural protein of said mixture as claimed in claim 7, wherein said protein is core protein of  ${f HIV}$ .
- 10. A structural protein of said mixture as claimed in claim 7, wherein said protein is p15 protein of  ${f HIV}.$
- 11. A structural protein of said mixture as claimed in claim 7, wherein said protein is p36 protein of  ${\bf HIV}$ .
- 12. A structural protein of said mixture as claimed in claim 7, wherein said protein is p42 protein of HIV.
- 13. A structural protein of said mixture as claimed in claim 7, wherein said protein is p80 protein of  ${f HIV}$ .
- 14. A mixture of labeled antigens of **Ruman Immunodeficiency Virus** (**HIV**), wherein said antigens are capable of being immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS); wherein said antigens comprise protein, glycoprotein, or a mixture thereof of **HIV**, and wherein said antigens are labeled with an immunoassay label selected from the group consisting of radioisotopes, enzymes, and fluorescent labels.
- 15. A labeled **antigen** of said mixture as claimed in claim 14, wherein said labeled **antigen** is in a purified form.
- 16. A labeled **antigen** of said mixture as claimed in claim 14, wherein said label is an enzyme or an enzyme substrate.
- 17. An extract of a retrovirus, which is **Ruman Immunodeficiency Virus** (**HIV**), wherein said extract comprises one a mixture of antigens of said retrovirus, wherein said antigens comprise protein, glycoprotein, or a mixture thereof of **HIV**, and said antigens are immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 18. Retroviral extract as claimed in claim 17, wherein said extract comprises p25 protein of said retrovirus.
- 19. Retroviral extract as claimed in claim 17, wherein said extract comprises pl5 protein of said retrovirus.
- 20. Retroviral extract as claimed in claim 17, wherein said extract comprises p25 protein of said retrovirus.
- 21. Retroviral extract as claimed in claim 17, wherein said extract comprises p36 protein of said retrovirus.
- 22. Retroviral extract as claimed in claim 17, wherein said extract comprises p80 protein of said retrovirus.
- 23. Retroviral extract as claimed in claim 17, wherein said extract comprises antigen that is not immunologically recognized by antibody which binds to p24 protein of Human T-Lymphotropic Virus (HTLV-1).

- 24. Retroviral extract as claimed in claim 17, wherein said extract is free from p19 protein of Human T-Lymphotropic Virus (HTLV-1) when assayed by indirect fluorescence assay using monoclonal **antibody** to said p19 protein.
- 25. Retroviral lysate as claimed in claim 24, wherein said lysate is enriched in p25 protein of said retrovirus.
- 26. Retroviral extract as claimed in claim 17, wherein said retrovirus has the identifying characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-232.
- 27. Retroviral extract as claimed in claim 17, wherein said retrovirus has the identifying characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-240.
- 28. Retroviral extract as claimed in claim 17, wherein said retrovirus has the identifying characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-241.
- 29. An in vitro diagnostic method for the detection of the quantity of the presence or absence of antibodies which bind to antigens of a human retrovirus indicative of Acquired Immune Deficiency Syndrome (AIDS) or of Lymphadenopathy-Associated Syndrome (pre-AIDS), wherein said method comprises contacting a lysate enriched in p25 protein of said retrovirus with a biological fluid for a time and under conditions sufficient for said p25 protein and antibodies in the biological fluid to form antigen-antibody complexes; and detecting the formation of said complexes.
- 30. The method of claim 29, wherein the detecting step further comprises measuring the formation of said **antigen-antibody** complex.
- 31. The method of claim 30, wherein formation of said antigen-antibody complex is measured by ELISA (an enzyme-linked immunoabsorbent assay) or indirect immunofluorescent assay.
- 32. The method of claim 29, wherein said biological fluid is human sera.
- 33. The method of claim 29, wherein said biological fluid is from a patient with AIDS.
- $34.\ \mbox{The method of claim 29, wherein said biological fluid is from a patient with pre-AIDS.$
- 35. The method of claim 29, wherein said human retrovirus is selected from the group consisting of Lymphadenopathy Associated Virus, LAV $_1$ ; Immune Deficiency Associated Virus, IDAV $_1$ ; and Immune Deficiency Associated Virus, IDAV $_2$ .
- 36. A diagnostic kit for the detection of the presence or absence of antibodies which bind to antigens of a human retrovirus indicative of Acquired Immune Deficiency Syndrome (AIDS) or of Lymphadenopathy-Associated Syndrome (pre-AIDS), wherein said kit comprises a lysate enriched in p25 protein of said retrovirus; a reagent to detect antigen-antibody immune complexes that comprise said protein; a biological reference material lacking antibodies that immunologically bind with said protein; a comparison sample comprising antibodies of said protein; and wherein said p25 protein and said reagent, biological reference material, and comparison sample are present in an amount sufficient to perform said detection.
- 37. The diagnostic kit of claim 36, wherein the formation of immune complexes is detected by employing immunological assays selected from the group consisting of radioimmunoassay, immunoenzymatic assay, and immunofluorescent assay.
- 38. The retrovirus according to claim 1, wherein said retrovirus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 39. The in vitro culture of **Human Immunodeficiency Virus** (**HIV**) according to claim 2, wherein said virus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 40. The isolate of a retrovirus according to claim 3, wherein said retrovirus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No.

- 41. The suspension of a retrovirus according to claim 4, wherein said retrovirus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 42. A mixture of antigens of **Ruman Immunodeficiency Virus** (**HIV**) according to claim 5, wherein said virus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 43. Antigen according to claim 6, wherein said virus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 44. Structural protein of **Human Immunodeficiency Virus** (**HIV**) according to any one of claims 7 to 9, wherein said virus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 45. Structural protein of **Human Immunodeficiency Virus** (**HIV**) according to any one of claims 10 to 13, wherein said virus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 46. A mixture of labeled antigens of **Human Immunodeficiency Virus** (**HIV**) according to claim 14, wherein said virus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 47. Retroviral lysate according to claim 25, wherein said retrovirus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 48. The method according to claim 29, wherein said retrovirus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.
- 49. The diagnostic kit according to claim 36, wherein said retrovirus has the identifying characteristics of a virus deposited under culture collection accession number selected from the group consisting of C.N.C.M. No. I-232, C.N.C.M. No. I-240, and C.N.C.M. No. I-241.

## L52 ANSWER 31 OF 41 USPATFULL on STN

92:48982 Method for detecting antibodies to human immunodeficiency virus. Friedman-Kien, Alvin, New York, NY, United States Yunzhen, Cao, New York, NY, United States Borkowsky, William, Brooklyn, NY, United States New York University, New York, NY, United States (U.S. corporation)

APPLICATION: US 1988-204871 19880610 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

US 5122446 19920616

- 1. A method for identifying the members of a human patient population that have been infected with <code>Ruman Immunodeficiency Virus</code> (HIV) which comprises: contacting a quantity of urine voided by a member of said patient population with an immunoreagent specific for detecting the presence in said urine of an <code>antibody</code> to at least one <code>HIV</code> protein, to form a complex, detecting the presence of said complex after said contacting step to obtain a result, comparing said result with a standard result which has been obtained by contacting with said immunoreagent urine of at least one human subject known to be free of <code>HIV</code> infection.
- 2. A method for determining whether a human subject has been infected with <code>Human Immunodeficiency Virus</code> (<code>HIV</code>) comprising the steps of: obtaining a urine sample from said human, assaying said sample by contacting at least an aliquot of said sample with an immunoreagent specific for detecting the presence of an <code>antibody</code> to at least one <code>HIV</code> protein in said sample to form a complex, detecting said complex after said contacting step to obtain a result, comparing said result of said assay with those of the same assay performed with urine from at

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3. A method for screening a human subject for exposure to <code>Ruman Immunodeficiency Virus</code> (<code>HIV</code>) comprising the steps of: obtaining a urine sample from said subject; assaying said sample by contacting at least an aliquot of said sample with an immunoreagent specific for detecting the presence of an <code>antibody</code> to at least one <code>HIV</code> protein to form a complex, detecting said complex, and determining whether said subject has been exposed to <code>HIV</code> based on the positive presence of at least one <code>antibody</code> of <code>HIV</code> in said sample.

- 4. A method for detecting the presence of antibodies to <code>Human Immunodeficiency Virus</code> (<code>HIV</code>) in a human subject comprising the steps of: obtaining a urine sample from said human subject; assaying said sample for the presence of at least one <code>antibody</code> to at least one <code>HIV</code> protein by contacting at least an aliquot of said sample with an immunoreagent specific for detecting the presence of said <code>antibody</code>, said protein being selected from the group consisting of p17, <code>p24</code> and combinations thereof.
- 5. The method of any one of claims 1-4 wherein said antibodies are directed against **Human Immunodeficiency Virus** viral protein **p24**, and said immunoreagent comprises an **antigen** immunochemically reactive with said antibodies.
- 6. The method of any one of claims 1-4 wherein said antibodies are directed against  ${\bf HIV}$  viral protein gp160 and said immunoreagent comprises an  ${\bf antigen}$  immunochemically reactive with said antibodies.
- 7. The method of any one of claims 1-4 wherein said antibodies are directed against  ${\bf HIV}$  viral protein gp120 and said immunoreagent comprises an  ${\bf antigen}$  immunochemically reactive with said antibodies.
- 8. The method of any one of claims 1-4 wherein said urine sample is less than one week old.
- 9. The method of any one of claims 1-4 wherein said immunoreagent comprises an **antigen** immunochemically reactive with an **antibody** raised against an **HIV** viral protein and specific for detecting antibodies to said protein.
- 10. The method of claim 9 wherein said antibodies are detected using an enzyme-linked immunosorbent assay.
- 11. The method of claim 9 wherein said antibodies are detected using Western blot.
- 13. The method of claim 9 wherein said antibodies are members of the group consisting of antibodies directed against HIV viral protein gp41 (anti-gp41), antibodies directed against HIV viral protein p24 (anti-p24) and combinations thereof and said specific immunoreagent respectively comprises an antigen selected from the group consisting of antigens immunochemically reactive with anti-gp41, antigens immunochemically reactive with anti-p24 and combinations of said antigens.

L52 ANSWER 32 OF 41 USPATFULL on STN 92:34051 Aids assay.

Croxson, Thomas S., Tenafly, NJ, United States
Beth Israel Medical Center, New York, NY, United States (U.S. corporation)
US 5108891 19920428

APPLICATION: US 1988-204568 19880609 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A method for analyzing a sample of a biological fluid with regard to the level of anti-p24 antibodies therein, comprising the steps of: (a) forming a mixture of: 1) the sample; and 2) an antigen solution containing free p24 antigen within a predetermined concentration range, the predetermined concentration range and the volumes of antigen solution and sample being chosen so that the initial concentration of free p24 antigen in the mixture is substantially equal to the concentration of free p24 antigen in the antigen solution; (b) incubating the mixture under conditions whereby anti-p24 antibodies from the sample, if any, can react with free p24 antigen to form antibody-antigen complexes; (c) assaying the mixture to obtain a concentration value for free p24 antigen in the mixture; (d) assaying a sample of the antigen solution to obtain a concentration value for free p24 antigen in the antigen solution;

obtained in step (d) and the concentration value obtained in step (c), said difference being indicative of the level of anti-p24 antibodies in the sample.

- 2. The method of claim 1 wherein the predetermined concentration range is from about 350 nanograms per liter to about 450 nanograms per liter.
- 3. The method of claim 2 wherein the mixture comprises by volume approximately 250 parts  ${\bf antigen}$  solution of 1 part sample.
- 4. The method of claim 2 wherein the predetermined concentration range is from about 380 nanograms per liter to about 425 nanograms per liter.
- 5. The method of claim 4 wherein the mixture comprises by volume approximately 250 parts **antigen** solution to 1 part sample.
- 6. A method for analyzing a biological fluid with regard to the levels of p24 antigen and anti-p24 antibodies therein, comprising the steps of: (a) forming a mixture of: 1) a first sample from the biological fluid; and 2) an antigen solution containing free p24 antigen within a predetermined concentration range, the predetermined concentration range and the volumes of antigen solution and first sample being chosen so that the initial concentration of free p24 antigen in the mixture is substantially equal to the concentration of free p24 antigen in the antigen solution; (b) incubating the mixture under conditions whereby anti-p24 antibodies from the first sample, if any, can react with free p24 antigen to form antibody-antigen complexes; (c) assaying the mixture to obtain a concentration value for **p24 antigen** in the mixture; (d) assaying a sample of the antigen solution to obtain a concentration value for free p24 antigen in the antigen solution; (e) determining the difference between the concentration value obtained in step (d) and the concentration value obtained in step (c), said difference being indicative of the level of anti-p24 antibodies in the biological fluid; and (f) assaying a second sample from the biological fluid for p24 antigen concentration; the assaying of steps (c), (d), and (f) being performed substantially simultaneously.
- 7. The method of claim 6 wherein the predetermined concentration range is from about 350 nanograms per liter to about 450 nanograms per liter.
- 8. The method of claim 8 wherein the mixture comprises by volume approximately 250 parts  ${\bf antigen}$  solution to 1 part first sample.
- 9. The method of claim 7 wherein the predetermined concentration range is from about 380 nanograms per liter to about 425 nanograms per liter.
- 10. The method of claim 9 wherein the mixture comprises by volume approximately 250 parts **antigen** solution to 1 part first sample.

L52 ANSWER 33 OF 41 USPATFULL on STN
91:96278 T-cell lymphotrophic virus protein and assay.
Essex, Myron E., Sharon, MA, United States
Allan, Jonathan S., Westwood, MA, United States
Lee, Tun-Hou, Newton, MA, United States
President and Fellows of Harvard College, Cambridge, MA, United States
(U.S. corporation)
US 5068174 19911126
APPLICATION: US 1988-250309 19881025 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. A method of assaying a biological specimen for the presence of HIV antibodies indicative of HIV infection, comprising the steps of: (a) incubating a biological specimen in which the presence of HIV antibodies is to be detected with a composition comprising a marker consisting essentially of i) p27 (a protein encoded by the open reading frame 3' to the env gene of HIV), or ii) a fragment of p27 having an antigenic determinant that reacts with anti-p27 antibody, said incubating being for a sufficient time and under conditions to allow said p27 polypeptide or fragment to form an immunocomplex with antibody present in said specimen; and (b) then determining whether an immunocomplex is formed between said marker and antibody in said specimen, the formation of an immunocomplex being indicative of the presence of HIV infection.
- 2. The method of claim 1, wherein said marker is labeled.
- 3. The method of claim 1, further comprising the step of reacting said specimen with an  ${f HIV}$  polypeptide lacking any antigenic determinant cross-reactive with said p27, for a sufficient time and under conditions

present in said specimen, and then determining whether an immunocomplex is formed between said HIV polypeptide and antibody in said specimen, the formation of an immunocomplex being indicative of the presence of HIV antibodies, other than p27-reactive antibodies, in the specimen.

- 4. The method of claim 3, wherein said  ${\tt HIV}$  polypeptide is a gag or env polypeptide.
- 5. The method of claim 4, wherein said **HIV** polypeptide is p55, **p24**, gp41, gp160, gp120 or pp17.
- 6. The method of claim 1 wherein said marker is substantially pure p27 or a substantially pure fragment thereof.
- 7. A method of detecting the presence of a p27 antigenic determinant in a biological specimen, comprising the steps of: (a) incubating said biological specimen with **antibody** having specificity against said antigenic determinant for a sufficient time and under conditions allowing the formation of an immunocomplex between said **antibody** and **antigen** in said specimen, and then determining whether an immunocomplex is formed, the formation of an immunocomplex being indicative of the presence of a p27 antigenic determinant in said specimen.
- 8. A kit for detecting **HIV antibody** comprising a container containing: a composition comprising marker consisting essentially of: i) p27 polypeptide (a protein encoded by the open reading frame 3' to the env gene of **HIV**), or ii) a fragment of p27 having an antigenic determinant that reacts with anti-p27 **antibody**; and means for determining formation of an immunocomplex between said marker and anti-p27 **antibody**.
- L52 ANSWER 34 OF 41 USPATFULL on STN
- 91:82139 Method and kit or detecting antibodies to antigens of **Human**Immunodeficiency Virus type 2 (HIV-2).

Montagnier, Luc, Le Plessis Robinson, France

Guetard, Denise, Paris, France

Brun-Vezinet, Francoise, Paris, France

Clavel, Francois, Paris, France

Institut Pasteur, Paris, France (non-U.S. corporation)

US 5055391 19911008

APPLICATION: US 1990-462353 19900103 (7)

PRIORITY: FR 1986-910 19860122

FR 1986-911 19860122

FR 1986-1635 19860206

FR 1986-1985 19860213

DOCUMENT TYPE: Utility; Granted. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. An in vitro diagnostic method for the detection of the presence or absence of human antibodies which bind to antigens of a human retrovirus, which is Ruman Immunodeficiency Virus Type 2 (HIV-2), indicative of Lymphadenopathy, wherein said antigens comprise protein antigen, glycoprotein antigen, peptide antigen, or a mixture thereof of HIV-2, and wherein said method comprises contacting antigens of HIV-2 with a biological fluid for a time and under conditions sufficient for the antigens and antibodies in the biological fluid to form antigen-antibody complexes, and detecting the formation of the complexes.
- 2. The method of claim 1, wherein the biological fluid is human serum.
- 3. The method of claim 1, wherein the biological fluid is from a patient with pre-AIDS.
- 4. The method of claim 1, wherein the human retrovirus is a human retroviral variant of LAV-2 which is cytopathic for human lymphocytes.
- 5. The method of claim 1, wherein the biological fluid is simultaneously contacted with a mixture of antigens comprising protein, glycoprotein, and peptides of Lymphadenopathy Associated Virus Type 1 (LAV-1) capable of binding to human antibodies, in an amount sufficient to detect the presence or absence of human antibodies which bind to antigens of LAV-1.
- 6. The method of claim 1, wherein the antigens comprise a lysate of HIV-2 and the antigens are capable of being immunologically recognized by serum of a patient afflicted with Lymphadenapathy Syndrome (LAS), Acquired Immune Deficiency Syndrome (AIDS), or AIDS Related Complex (ARC).

protein or glycoprotein of **HIV-2** selected from the group consisting of p16, **p26**, gp 36, and gp 130-140.

- 8. The method of claim 1, wherein the antigens comprise p16 and  ${\bf p26}$  proteins of  ${\bf HIV-2}$ .
- 9. The method of claim 1, wherein the antigens comprise gp 36 glycoprotein of **HIV-**2.
- 10. The method of claim 1, wherein the antigens comprise gp 130-140 glycoprotein of  ${\bf HIV}-2$ .
- 11. The method of claim 1, wherein the antigens comprise  ${\bf p26}$  protein and gp36 glycoprotein of  ${\bf HIV}{\text{-}}2$ .
- 12. The method of claim 1, wherein the antigens comprise  ${\bf p26}$  protein and gp 36 glycoprotein and gp 130-140 glycoprotein of  ${\bf HIV}$ -2.
- 13. The method of claim 1, wherein the antigens comprise pl6 and p26 proteins and gp 130-140 glycoproteins of HIV-2.
- 14. The method of claim 1, wherein the biological fluid is also contacted with antigens indicative of **Ruman Immunodeficiency Virus** Type 1 (**HIV-**1), which are capable of binding to human antibodies, in an amount sufficient to detect the presence or absence of human antibodies which bind to antigens of **HIV-**1, wherein said antigens comprise protein **antigen**, glycoprotein **antigen**, peptide **antigen**, or a mixture thereof indicative of **HIV-**1.
- 15. The method of claim 14, wherein the antigens of HIV-1 are selected from the group consisting of p18, p25, gp 41-43, gp 110/120, and mixtures thereof, of HIV-1.
- 16. The method of claim 14, wherein the antigens of  ${\bf HIV}{ ext{-}}{\bf 1}$  comprise p25 and gp 41 of  ${\bf HIV}{ ext{-}}{\bf 1}$ .
- 17. The method of claim 14, wherein the antigens are isolated from lysates of  ${\bf HIV}{-}1$  and  ${\bf HIV}{-}2$  by affinity chromatography and fixed to a water-insoluble support.
- 18. The method of claim 1, wherein the antigens are fixed to a water-insoluble support.
- 19. The method of claim 1, wherein the antigens are fixed to water-insoluble spheres.
- $20.\ \mbox{The method of claim 1, wherein the antigens are fixed to water-insoluble agarose spheres.$
- 21. The method of claim 1, wherein the antigens are fixed to wells of a titration microplate.
- 22. The method of claim 1, wherein the antigens do not immunologically cross-react with pl9 protein or **p24** protein of human T-lymphotropic virus type 1 (HTLV-I) or of human T-Lymphotropic virus type 2 (HTLV-II).
- 23. A diagnostic kit for the detection of the presence or absence of human antibodies which bond to antigens of **Human Immunodeficiency Virus** Type 2 (**HIV**-2) indicative of lymphadenopathy, wherein said antigens comprise protein **antigen**, glycoprotein **antigen**, peptide **antigen**, or a mixture thereof, and wherein said kit comprises antigens of **HIV**-2, a reagent to detect **antigen**-antibody complexes that comprise said antigens, a biological reference material lacking antibodies that immunologically bind with said antigens, a comparison sample comprising antibodies of **HIV**-2, and wherein said antigens, reagent, and biological reference material are present in an amount sufficient to perform said detection.
- 24. The diagnostic kit of claim 23, wherein said immune complexes are detected by employing immunological labels selected from the group consisting of radioisotopes, enzymes, and fluorescent labels.
- 25. The diagnostic kit of claim 23, wherein said kit also contains antigens of Lymphadenopathy Associated Virus Type 1 (LAV-1), wherein said antigens comprise a mixture of protein, glycoprotein, and peptides of Lymphadenopathy Associated Virus Type 1 (LAV-1) capable of binding to human antibodies, in an amount sufficient to detect the presence or absence of human antibodies which bind to antigens of LAV-1.
- 26. An in vitro diagnostic method for the detection of the presence or absence of human antibodies which bind to antigens indicative of a human retrovirus, which is **Human Immunodeficiency Virus** Type 2

glycoprotein antigen, peptide antigen, or a mixture thereof indicative of HIV-2, and wherein said method comprises contacting said antigens with a biological fluid for a time and under conditions sufficient for the antigens and antibodies in the biological fluid to form an antigen-antibody complex, wherein said antigens are substantially free of viral particles, and detecting the formation of the complex.

- 27. The method of claim 26, wherein the biological fluid is human serum.
- 28. The method of claim 26, wherein the antigen is a peptide.
- 29. The method of claim 26, wherein the antigen is a glycoprotein.
- 30. The method of claim 26, wherein said **antigen** is labeled with a immunoassay label selected form the group consisting of radioisotopes, enzymes, and fluorescent labels.
- 31. The method of claim 26, wherein the human retrovirus is LAV-2.
- 32. The method of claim 21, wherein the human retrovirus is a human retroviral variant of LAV-2 which is cytopathic for human lymphocytes.
- 33. The method of claim 26, wherein the antigens are derived from a retrovirus having the characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-502.
- 34. The method of claim 26, wherein the antigens are derived from a retrovirus having the characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-532.
- 35. The method of claim 26, wherein the antigens comprise an extract of HIV-2, and the antigens are capable of being immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS), Acquired Immune Deficiency Syndrome (AIDS), or AIDS Related Complex (ARC).
- 36. The method of claim 26, wherein the **antigen** is an external envelope protein of **HIV-**2.
- $37.\ \mbox{The method of claim 26, wherein the $antigen$ is a transmembrane protein.}$
- 38. The method of claim 26, wherein the **antigen** is a major core protein of **HIV-**2.
- 39. The method of claim 26, wherein the **antigen** is a core protein of **HIV-2**, other than a major core protein of **HIV-2**.
- 40. The method of claim 26, wherein the antigens comprise at least one protein or glycoprotein of **HIV-**2 selected from the group consisting of p16, **p26**, gp 36, and gp 130-140.
- 41. The method of claim 26, wherein the antigens comprise pl6 and p26 proteins of HIV-2.
- 42. The method of claim 26, wherein the antigens comprise gp 36 glycoprotein of **HIV-**2.
- 43. The method of claim 26, wherein the antigens comprise gp 130-140 glycoprotein of  ${\bf HIV}-2$ .
- 44. The method of claim 26, wherein the antigens comprise p26 protein and gp36 glycoprotein of HIV-2.
- 45. The method of claim 26, wherein the antigens comprise  $\bf p26$  protein and gp 36 glycoprotein and gp 130-140 glycoprotein of  $\bf HIV$ -2.
- 46. The method of claim 26, wherein the antigens comprise pl6 and **p26** proteins and gp 130-140 glycoproteins of **HIV-**2.
- 47. The method of claim 26, wherein the biological fluid is also contacted with antigens indicative of **Ruman Immunodeficiency Virus** Type 1 (**HIV-1**), which are capable of binding to human antibodies, in an amount sufficient to detect the presence or absence of human antibodies which bind to antigens of **HIV-1**.
- 48. The method of claim 47, wherein the antigens of HIV-1 are selected from the group consisting of p18, p25, gp 41-43, gp 110/120, and mixtures thereof, of HIV-1.
- 49. The method of claim 26, wherein the antigens are from disrupted

50. A diagnostic kit for the detection of the presence or absence of human antibodies which bind to antigens indicative of **Human**Immunodeficiency Virus Type 2 (HIV-2), wherein said antigens comprise protein antigen, glycoprotein antigen, peptide antigen, or a mixture thereof indicative of HIV-2, and wherein said kit comprises said antigens, a reagent to detect antigen-antibody complexes that comprise said antigens, a biological reference material lacking antibodies that immunologically bind with said antigens, a comparison sample comprising antibodies of HIV-2, and wherein said antigens, reagent, and biological reference material are present in an amount sufficient to perform said detection.

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- 51. The kit of claim 50, wherein the antigen is a peptide.
- 52. The kit of claim 50, wherein the antigen is a glycoprotein.
- 53. The kit of claim 50, wherein said **antigen** is labeled with an immunoassay label selected from the group consisting of radioisotopes, enzymes, and fluorescent labels.
- 54. The kit of claim 50, wherein the antigens comprise an extract or a lysate of HIV-2, and the antigens are capable of being immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS), Acquired Immune Deficiency Syndrome (AIDS), or AIDS Related Complex (ARC).
- 55. The kit of claim 50, wherein the **antigen** is an external envelope protein of **HIV-**2.
- 56. The kit of claim 50, wherein the antigen is a transmembrane protein.
- 57. The kit of claim 50, wherein the **antigen** is a major core protein of **HIV-**2.
- 58. The kit of claim 50, wherein the **antigen** is a core protein of **HIV-**2, other than a major core protein of **HIV-**2.
- 59. The kit of claim 50, wherein the antigens comprise at least one protein or glycoprotein of HIV-2 selected from the group consisting of p16, p26, gp 36, and gp 130-140.
- 60. The kit of claim 50, wherein the antigens comprise p16 and  ${\bf p26}$  proteins of  ${\bf HIV}{\text{-}}2$ .
- 61. The kit of claim 50, wherein the antigens comprise gp 36 glycoprotein of  ${\bf HIV-}2$ .
- 62. The kit of claim 50, wherein the antigens comprise gp 130-140 glycoprotein of  ${f HIV}-2$ .
- 63. The kit of claim 50, wherein the antigens comprise **p26** protein and gp 36 glycoprotein of **HIV-**2.
- 64. The kit of claim 50, wherein the antigens comprise  $\bf p26$  protein and gp 36 glycoprotein and gp 130-140 glycoprotein of  $\bf HIV-2$ .
- 65. The kit of claim 50, wherein the antigens comprise pl6 and p26 proteins and gp 130-140 glycoproteins of HIV-2.
- 66. The kit of claim 50, wherein said kit also comprises antigens indicative of **Human Immunodeficiency Virus** Type 1 (**HIV**-1), which are capable of binding to human antibodies, in an amount sufficient to detect the presence or absence of human antibodies which bind to antigens of **HIV**-1, wherein said antigens comprise a mixture of protein **antigen**, glycoprotein **antigen**, and peptide **antigen** indicative of **HIV**-1.
- 67. The kit of claim 66, wherein the antigens of HIV-1 are selected from the group consisting of p18, p25, gp 41-43, gp 110/120, and mixtures thereof, of HIV-1.
- 68. The kit of claim 50, wherein the antigens are fixed to a water-insoluble support.
- $69.\ \mbox{The kit}$  of claim  $50,\ \mbox{wherein}$  the antigens are fixed to water-insoluble spheres.
- 70. The kit of claim 50, wherein the antigens are fixed to water-insoluble agarose spheres.
- 71. The kit of claim 50, wherein the antigens are fixed to wells of a titration microplate.

- 72. The kit of claim 66, wherein the antigens are isolated from lysates of  ${\tt HIV-1}$  and  ${\tt HIV-2}$  by affinity chromatography and fixed to a water-insoluble support.
- 73. The kit of claim 50, wherein the antigens do not immunologically cross-react with p19 protein or  $\bf p24$  protein of human T-lymphotropic virus type 1 (HTLV-I) or of human T-lymphotropic virus type 2 (HTLV-II).
- 74. The kit of claim 50, wherein the antigens are from disrupted whole virus particles present in the lysate or isolated therefrom.

#### L52 ANSWER 35 OF 41 USPATFULL on STN

91:54855 Retrovirus capable of causing AIDS, antigens obtained from this retrovirus and corresponding antibodies and their application for diagnostic purposes.

Montagnier, Luc, Le Plessis Robinson, France

Guetard, Denise, Paris, France

Brun-Vezinet, Francoise, Paris, France

Clavel, Francois, Paris, France

Institut Pasteur, Paris, France (non-U.S. corporation)

US 5030718 19910709

## APPLICATION: US 1990-462984 19900110 (7)

PRIORITY: FR 1986-910 19860122

FR 1986-911 19860122

FR 1986-1635 19860206

FR 1986-1985 19860213

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. An antibody formed against human immunodeficiency virus type
- 2 (HIV-2), wherein the antibody is in biologically pure form.
- 2. The **antibody** as claimed in claim 1, wherein the **antibody** is formed against pl6 protein specific to **HIV-**2, or peptides derived from said protein.
- 3. The **antibody** as claimed in claim 1, wherein the **antibody** is formed against **p26** protein specific to **HIV-**2, or peptides derived from said protein.
- 4. The **antibody** as claimed in claim 1, wherein the **antibody** is formed against gp36 glycoprotein of **HIV-2**, or peptides derived from said glycoprotein.
- 5. The **antibody** as claimed in claim 1, wherein the **antibody** is formed against gp130-140 glycoprotein of **HIV**-2, or peptides derived from said glycoprotein.
- 6. The antibody as claimed in claim 1, which is a polyclonal antibody.
- 7. The antibody as claimed in claim 1, which is a monoclonal antibody.
- 8. An **antibody** that is formed against an immunological complex, wherein the complex comprises an **antigen** of **Human Immunodeficiency Virus** Type 2 (**HIV-**2) and **antibody** to said **antigen**.
- L52 ANSWER 36 OF 41 USPATFULL on STN
- 91:54693 Membrane-strip reagent serodiagnostic apparatus and method. Clemmons, Roger M., Gainesville, FL, United States

University of Florida, Gainesville, FL, United States (U.S. corporation) US 5030555 19910709

APPLICATION: US 1988-243257 19880912 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A serodiagnostic device comprising (A) a porous membrane that presents a first surface and an opposing second surface, wherein a first immunoreagent is bound to said second surface and is capable of binding a foreign analyte to form a complex when said foreign analyte is brought into contact with said first immunoreagent by exposing said first surface to a sample containing said foreign analyte; (B) a matrix that presents a first surface and an opposing second surface and that contains a second immunoreagent which is labeled and which is capable of binding said foreign analyte to form a labeled complex when said foreign analyte is sandwiched between said first immunoreagent and said second immunoreagent, wherein (i) said first surface of said matrix is adjacent to said second surface of said membrane, (ii) said matrix is wettable by or soluble in an aqueous fluid, and (iii) second immunoreagent is mobilized when said matrix is wetted; and (C) a support upon which said matrix and said membrane are provided such that said second surface of

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- 2. A serodiagnostic device according to claim 1, wherein each of said first and second immunoreagents comprises monoclonal or polyclonal antibody.
- 3. A serodiagnostic device according to claim 1, wherein said foreign analyte is selected from the group consisting of human choriogonadotropin, a hepatitis B surface antigen and a HIV-associated antigen.
- 4. A serodiagnostic device according to claim 1, wherein said foreign analyte is an **HIV antibody**.
- 5. A serodiagnostic device according to claim 4, wherein said HIV antibody is an anti-p24 antibody.
- 6. A serodiagnostic device according to claim 1, wherein each of said first and second immunoreagents is an **antigen**.
- $7.\ A$  serodiagnostic device according to claim 8, wherein said antigen is an HIV antigen.
- 8. A serodiagnostic device according To claim 7, wherein said  ${\bf HIV}$  antigen is  ${\bf p24}\,.$
- 9. A serodiagnostic device according to claim 1, wherein said device comprises a plurality of test pads provided on said support and wherein at least a first test pad of said plurality is comprised of (i) a porous membrane that presents a first surface and an opposing second surface, wherein a first immunoreagent is bound to said second surface and is capable of binding a foreign analyte to form a complex when said foreign analyte is brought into contact with said first immunoreagent by exposing said first surface to a sample containing said foreign analyte; (ii) a matrix that presents a first surface and an opposing second surface and that contains a second immunoreagent which is labeled and which is capable of binding said foreign analyte to form a labeled complex when said foreign analyte is sandwiched between said first immunoreagent and said second immunoreagent, wherein (a) said first surface of said matrix is adjacent to said second surface of said membrane, (b) said matrix is wettable by or soluble in an aqueous fluid, and (c) second immunoreagent is mobilized when said matrix is wetted.
- 10. A serodiagnostic device according to claim 9, wherein at least one other test pad of said plurality provides a positive or negative control relative to said first test pad.
- $11.\ A$  serodiagnostic device according to claim 1, wherein said second immunoreagent is labeled with an enzyme.
- 12. A method for serodiagnosis of a fluid sample, comprising the steps of (A) inserting a serodiagnostic device according to claim 1 into a sample of test fluid containing said foreign analyte such that said sample contacts said membrane, whereby said foreign analyte (i) traverses said first surface of said membrane to said second surface of said membrane and binds said first immunoreagent and (ii) mobilizes said second immunoreagent; then (B) inserting said serodiagnostic device into a washing solution such that saId solution contacts said membrane, whereby said second immunoreagent not bound to said complex is removed from said matrix; and thereafter (C) inserting said serodiagnostic device into a solution of a compound that reacts with saId labeled complex to produce a detectable reaction product.
- 13. A method according to claim 12, wherein said serodiagnostic device comprises a plurality of test pads provided on said support and wherein at least one test pad of said plurality is comprised of (i) a porous membrane that presents a first surface and an opposing second surface, wherein a first immunoreagent is bound to said second surface and is capable of binding a foreign analyte to form a complex when said foreign analyte is brought into contact with said first immunoreagent by exposing said first surface to a sample containing said foreign analyte; (ii) a matrix that presents a first surface and an opposing second surface and that contains a second immunoreagent which is labeled and which is capable of binding said foreign analyte to form a labeled complex when said foreign analyte is sandwiched between firs immunoreagent and said second immunoreagent, wherein (a) said first surface of said matrix is adjacent to said second surface of said membrane, (b) said matrix is wettable or by soluble in an aqueous fluid, and (c) second immunoreagent is mobilized when said matrix is wetted.
- 14. A method according to claim 13, wherein said reaction product is detectable by visual observation of said serodiagnostic device after step (C).

- 15. A method according to claim 12, wherein said test fluid is human urine.
- 16. A method according to claim 12, wherein said test fluid is human serum or whole blood.
- 17. A method according to claim 12, wherein said reaction product indicates the presence of human choriogonadotropin, a hepatitis B surface antigen or a HIV-associated antigen.
- 18. A method according to claim 17, wherein said reaction product indicates the presence of **p24 antigen**.
- 19. A method according to claim 12, wherein said reaction product indicates the presence of an **HIV antibody**.
- 20. A method according to claim 19, wherein said **HIV antibody** is anti-p24 antibody.
- L52 ANSWER 37 OF 41 USPATFULL on STN
- 91:3024 Immunoassay for  ${\bf HIV}{\rm -I}$  antigens using F(AB') $_2$  fragments as probe. Stewart, James L., Buffalo Grove, IL, United States

Ketchum, Susan K., Libertyville, IL, United States

Stumpf, Robert J., Chicago, IL, United States

Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)

US 4983529 19910108

APPLICATION: US 1988-204799 19880610 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. An immunoassay for the detection of **HIV** 1 antigens in a biological sample comprising forming an **antibody/antigen** complex wherein the **antibody** portion of said complex comprises anti-**HIV** 1  $F(ab')_2$  fragments, and detecting the presence or amount of the **antibody/antigen** complex formed.
- 2. The immunoassay of claim 1 wherein the presence or amount of the antibody/antigen complex formed is determined by incubating said complex with a labeled, anti-species antibody specific for said anti-HIV 1 fragments.
- 3. The immunoassay of claim 2 wherein said anti-species antibody comprises  $F(ab')_2$  fragments.
- 4. The immunoassay of claims 2 or 3 wherein said label comprises a radioisotope, enzyme, fluorescent compound, chemiluminescent compound, or member of a specific binding pair.
- 5. The immunoassay of claim 3 wherein said **antibody** portion of said complex further comprises anti-HIV 1 **antibody** bound on a solid support.
- 6. The immunoassay of claim 5 wherein said bound anti-HIV 1 antibody comprises at least one monoclonal antibody.
- 7. The immunoassay of claim 6 wherein said bound anti-HIV 1 antibody comprises the monoclonal antibodies designated 31-42-19 and 31-90-25 deposited at the ATCC under accession numbers HB 9726 and HB 9725, respectively.
- 8. The immunoassay of claim 5 wherein said bound anti-HIV 1 antibody comprises a polyclonal anti-HIV 1.
- 9. The immunoassay of claims 6, 7 or 8 wherein said bound antibody further comprises  $F(ab')_2$  fragments.
- 10. An immunoassay for the detection of HIV 1 p24 antigen in a biological sample comprising the steps of: a. coating a solid support with a monoclonal antibody mixture derived from a first animal species; b. contacting the coated support with the sample, incubating and washing; c. contacting the support with a probe comprising anti-HIV 1 F(ab')<sub>2</sub> fragments from a second animal species, incubating and washing; d. contacting the support with labeled F(ab')<sub>2</sub> fragments specific for said probe, incubating and washing; e. contacting the support with an o-phenylenediamine-hydrogen peroxide solution; and f. measuring the absorbance of the color product formed at 492 nm to determine the presence of HIV 1 p24 in the sample; wherein said monoclonal antibody mixture comprises the monoclonal antibodies designated 31-42-19 and 31-90-25 deposited at the ATCC under accession numbers HB 9726 and HB 9725, respectively.
- 11. An immunoassay for the detection of HIV 1 antigens in a biological

cample complicing one scope of a. coulting a solic support nic. anti-HIV 1 antibody from a first animal species; b. contacting the coated support with the sample, incubating and washing; c. contacting the support with a probe comprising anti-HIV 1 F(ab')2 fragments from a second animal species, incubating and washing; d. contacting the support with labeled F(ab')2 fragments specific for said probe, incubating and washing; e. contacting the support with an o-phenylenediamine-hydrogen peroxide solution; and f. measuring the absorbance of the color product formed at 492 nm to determine the presence of HIV 1 antigens in the sample.

- 12. A dignostic reagent for the detection of HIV 1 antigens comprising anti-HIV 1 F(ab')<sub>2</sub> fragments.
- 13. A diagnostic kit for the detection of  $\boldsymbol{\mathtt{HIV}}$  1 antigens comprising the diagnostic reagent of claim 12.
- 14. A diagnostic kit for the detection of HIV 1 p24 antigen comprising anti-HIV 1  $F(ab')_2$  fragments and the monoclonal antibodies designated 31-42-19 and 31-90-25 deposited at the ATCC under accession numbers HB 9726 and HB 9725, respectively.

L52 ANSWER 38 OF 41 USPATFULL on STN 89:100563 Monoclonal antibody specific to HIV antigens. Kortright, Kenneth H., Cooper, FL, United States Hofheinz, David E., Miami, FL, United States Sullivan, Carole, Miami, FL, United States Toedter, Gary P., Miramar, FL, United States Coulter Corporation, United States (U.S. corporation) US 4888290 19891219 APPLICATION: US 1987-118145 19871106 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

What is claimed is:

- 1. A hybridoma cell line which produces a monoclonal antibody which specifically binds to an epitope of the KC-57 antigen and is on deposit with the American Type Culture Collection, Rockville, Md., and assigned A.T.C.C. No. HB 9585.
- 2. A monoclonal antibody produced from the hybridoma cell line sample on deposit with the American Type Culture Collection, Rockveille, Md. and assigned A.T.C.C. No. HB 9585.
- 3. A monoclonal antibody which specifically binds to an antigenic determinant of the HIV p55, p24, p39 and p33 core antigens identified as KC-57, and which monoclonal  $\boldsymbol{antibody}$  does not have binding specificity with respect to the HIV core antigen pl8 and HIV envelope antigens.

L52 ANSWER 39 OF 41 USPATFULL on STN 89:98908 Enzyme immunoassay for detecting HIV antigens in human sera. Kortright, Kenneth H., Cooper City, FL, United States Hofheinz, David E., Homestead, FL, United States Forman, Meryl A., Miami, FL, United States Lee, Song Y., Plantation, FL, United States Smariga, Paulette E., N. Miami, FL, United States Stoner, Candie S., Hollywood, FL, United States Coulter Corporation, Hialeah, FL, United States (U.S. corporation) US 4886742 19891212 APPLICATION: US 1987-118149 19871106 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

What is claimed is:

1. An immunoassay for detecting HIV antigens in a human physiological fluid test sample containing cells and which sample may have circulating  $\ensuremath{\mathbf{antigen}},\ \ensuremath{\mathsf{said}}\ \ensuremath{\mathsf{assay}}\ \ensuremath{\mathsf{comprising:}}\ \ensuremath{\mathsf{(a)}}\ \ensuremath{\mathsf{introducing}}\ \ensuremath{\mathsf{into}}\ \ensuremath{\mathsf{contact}}\ \ensuremath{\mathsf{with}}\ \ensuremath{\mathsf{a}}$ solid surface to which is bound a known quantity of a monoclonal antibody capable of binding to a common epitope of the HIV p55, p24, p39 and p33 core antigens and without binding the HIV p18 core antigen and HIV envelope antigens, a predetermined volume of the test sample; (b) incubating said test sample in contact with said surface to form resultant antigen-antibody complexes; and (c) incubating the resultant complexes and subjecting same to a labelled human anti-HIV antibody conjugate which is capable of yielding a quantitatively measurable signal correlated to the signal for a normal negative test sample to indicate either antigen positive or negative for the test sample with picogram sensitivity of at least approximately 7.8 picograms per milliliter of test sample within a period of approximately four hours from the time of commencement of the immunoassay.

the test sample and said surface of step (a) of a lysing reagent for uniformly releasing antigens available from said cells during incubation.

- 3. The immunoassay of claim 1 in which said antibody of step (c) is labelled with an enzyme which is capable of producing the said signal when contacted with an enzyme substrate.
- 4. The immunoassay of claim 1 in which said monoclonal **antibody** is the KC=57 monoclonal **antibody** produced from a hybridoma cell line having the identifying characteristics of the cell line samples on deposit with the American Type Culture Collection, Rockville, Md., and assigned A.T.C.C. deposit No. HB 9585 producing mouse IgGl monoclonal **antibody** to the KC-57 **antigen**.
- 5. The immunoassay of claim 1 in which the labelled human anti-HIV antibody conjugate of step (c) is a glycoprotein bound antibody conjugate labelled with an enzyme capable of producing a color detection signal when contacted with an enzyme substrate.
- 6. The immunoassay of claim 5 in which said conjugate is a biotinylated  ${\bf antibody}$ .
- 7. A kit for use in performing an immunoassay for detecting  ${f HIV}$ antigens in a physiological fluid test sample comprising in combination: (a) a solid surface to which is bound a known quantity of the KC-57 monoclonal antibody capable of binding with a common epitope of the HIV p55, p24, p39 and p33 core antigens and which does not specifically bind to the HIV pl8 core antigen and HIV envelope antigens; (b) a container containing an amount of a labelled human anti-HIV antibody conjugate for providing a useful detectible signal for a test sample; (c) a container containing an amount of a lysing agent for uniformly releasing viral antigens which may be present in cells in a test sample; and (d) containers of incubating and washing reagents necessary for visualizing immunological reactions resulting from use of the kit in performing the immunoassay said combination selected quantitatively to obtaining such visual immunological reactions at picogram sensitivity within a period of approximately four or less hours from the time of commencement of said immunoassay.
- 8. The kit described in claim 7 in which said monoclonal **antibody** is the KC-57 monoclonal **antibody** produced from a hybridoma cell line which has the identifying characteristics of the hybridoma cell line samples on deposit with the American Type Culture Collection, Rockville, Md. and assigneed A.T.C.C. deposit No. HB 9585.
- 9. An immunoassay for detectinng HIV antigens in a human physiological fluid test sample containing cells and which sample may have circulating antigen, said assay comprising: (a) introducing into contact with a solid surface to which is bound a known quantity of a monoclonal antibody capable of binding to a common epitope of the HIV core antigens p55, p24, p39 and p33 without binding to the HIV core  ${\tt antigen}$  p18 or  ${\tt HIV}$  envelope antigens, a predetermined volume of the test sample and a known quantity of a lysing reagent for uniformly releasing antigens available from said cells during incubation; (b) incubating said test sample and lysing reagent in contact with said surface to form resultant antigen-antibody complexes; and (c) incubating the resultant complexes and subjecting same to a labelled human anti-HIV antibody conjugate which is capable of producing a quantitatively measurable signal at picogram sensitivity of at least approximately 7.8 picograms per milliliter of test sample correlated to the signal for a normal negative test sample to indicate either antigen positive or negative for the test sample within a period of approximately four hours from the time of commencement of the immunoassay.
- 10. The immunoassay of claim 9 in which said human anti-HIV antibody conjugate of step (c) is labelled with an enzyme capable of producing said signal when contacted with an enzyme substrate.
- 11. The immunoassay of claim 9 in which said monoclonal **antibody** has the binding specificity characteristics of the monoclonal **antibody** produced by the hybridoma cell line on deposit with the American Type Culture Collection, Rockville, Md., A.T.C.C. deposit No. HB 9585.
- 12. The immunoassay of claim 9 in which said conjugate is a biotinylated  ${\bf antibody}$ .

Montagnier, Luc, Robinson, France
Guetard, Denise, Paris, France
Brun-Vezinet, Francoise, Paris, France
Clavel, Francois, Paris, France
Institut Pasteur, Paris, France (non-U.S. corporation)
US 4839288 19890613

APPLICATION: US 1986-835228 19860303 (6)
PRIORITY: FR 1986-910 19860122
FR 1986-911 19860122
FR 1986-1635 19860206
FR 1986-1985 19860213
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:

- 1. A human retrovirus, wherein the retrovirus is **Human**Immunodeficiency Virus Type 2 (HIV-2) in a biologically pure form.
- 2. An in vitro culture of **Human Immunodeficiency Virus** Type 2 (**HIV-**2) as claimed in claim 1.
- 3. A suspension of **Ruman Immunodeficiency Virus** Type 2 (**HIV-**2) as claimed in claim 1 in a buffer therefor, wherein the suspension comprises protein **antigen**, glycoprotein **antigen**, or a mixture of protein and glycoprotein antigens of the retrovirus and the **antigen** is capable of being immunologically recognized by serum of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 4. A labeled antigen of Human Immunodeficiency Virus Type 2 (HIV-2) as claimed in claim 1, wherein the antigen is protein antigen, glycoprotein antigen, or a mixture of protein and glycoprotein antigens, and the antigen is capable of being immunologically recognized by sera of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS); and wherein said antigen is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 5. A supernatant of a cell culture infected with **Ruman**Immunodeficiency Virus Type 2 as claimed in claim 1, wherein the supernatant comprises protein antigen, glycoprotein antigen, or a mixture of protein and glycoprotein antigens of the retrovirus and the antigen is capable of being immunologically recognized by serum of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 6. A composition containing at least one protein or glycoprotein of **Human Immunodeficiency Virus** Type 2 (**HIV-**2) as claimed in claim 1, free of human cells and of other LAV-II proteins.
- 7. Human retrovirus as claimed in claim 1, wherein said retrovirus is cytopathic to human T4 lymphocytes and is comprised of proteins or glycoproteins that are immunologically cross-reactive with antibodies to proteins and glycoproteins of LAV-II.
- 8. Antigen of Ruman Immunodeficiency Virus Type 2 (HIV-2), wherein the antigen is protein antigen, glycoprotein antigen, or a mixture of protein and glycoprotein antigens and the antigen is free of human cells and of other LAV-II proteins and is capable of being immunologically recognized by serum of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 9. Antigen as claimed in claim 8, wherein the antigen is a protein.
- 10. Antigen as claimed in claim 9, wherein the antigen is an external envelope protein.
- 11. **Antigen** as claimed in claim 9, wherein the **antigen** is a transmembrane protein.
- 12. Antigen as claimed in claim 9, wherein the antigen is a major core protein.
- 13. **Antigen** as claimed in claim 9, wherein the **antigen** is a core protein, other than a major core protein.
- 14. An immunological complex between the **antigen** of claim 8 and an **antibody** recognizing said **antigen**.
- 15. The immunological complex of claim 14, wherein the complex is labeled with an immunoassay label selected from the group consisting of

radioaccito, chirimatro, and radioaccito raport.

- 16. The immunological complex of claim 14, wherein said antigen comprises a major core protein of said virus.
- 17. The immunological complex of claim 16, wherein the complex is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 18. **Antigen** as claimed in claim 8, wherein the **antigen** is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 19. **Antigen** as claimed in claim 10, wherein the **antigen** is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 20. **Antigen** as claimed in claim 11, wherein the **antigen** is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 21. **Antigen** as claimed in claim 12, wherein the **antigen** is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 22. **Antigen** as claimed in claim 13, wherein the **antigen** is labeled with an immunoassay label selected from the group consisting of radioactive, enzymatic, and fluorescent labels.
- 23. An extract of **Human Immunodeficiency Virus** Type 2 (**HIV**-2), wherein the extract comprises protein **antigen**, glycoprotein **antigen**, or a mixture of protein and glycoprotein antigens of the retrovirus and the **antigen** is free of human cells and of other LAV-II proteins and is capable of being immunologically recognized by serum of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 24. Retroviral extract as claimed in claim 23, wherein the extract contains external envelope protein of said retrovirus.
- 25. Retroviral extract as claimed in claim 23, wherein the extract contains transmembrane protein of said retrovirus.
- 26. Retroviral extract as claimed in claim 23, wherein the extract contains major core protein of said retrovirus.
- 27. Retroviral extract as claimed in claim 23, wherein the extract contains core protein other than major core protein of said retrovirus.
- 28. A lysate of **Human Immunodeficiency Virus** Type 2 (**HIV-2**), wherein the lysate comprises protein **antigen**, glycoprotein **antigen**, or a mixture of protein and glycoprotein antigens of the retrovirus and the **antigen** is free of human cells and of other LAV-II proteins and is capable of being immunologically recognized by serum of a patient afflicted with Lymphadenopathy Syndrome (LAS) or Acquired Immune Deficiency Syndrome (AIDS).
- 29. Retroviral lysate as claimed in claim 28, wherein the lysate comprises external envelope protein of said retrovirus.
- 30. Retroviral lysate as claimed in claim 28, wherein the lysate comprises transmembrane protein of said retrovirus.
- 31. Retroviral lysate as claimed in claim 28, wherein the lysate comprises major core protein of said retrovirus.
- 32. Retroviral lysate as claimed in claim 28, wherein the lysate comprises core protein other than major core protein of said retrovirus.
- 33. Supernatant as claimed in claim 5, wherein the supernatant comprises external envelope protein of said retrovirus.
- 34. Supernatant as claimed in claim 5, wherein the supernatant comprises transmembrane protein of said retrovirus.
- 35. Supernatant as claimed in claim 5, wherein the supernatant comprises major core protein of said retrovirus.
- 36. Supernatant as claimed in claim 5, wherein the supernatant comprises core protein other than major core protein of said retrovirus.
- 37. Composition as claimed in claim 6, wherein the composition contains proteins of Lymphadenopathy Associated Virus Type 1 (LAV-1),  $\frac{1}{2}$

LAV-1.

- 38. Composition as claimed in claim 6, wherein the composition contains at least one protein or glycoprotein of said virus selected from the group consisting of p16, **p26**, gp36, and gp130-140.
- 39. Composition as claimed in claim 6, wherein the composition contains **p26** protein and qp36 qlycoprotein of said virus.
- 40. Composition as claimed in claim 6, wherein the composition contains  ${\bf p26}$  protein and gp36 glycoprotein and gp 130-140 glycoprotein of said virus.
- 41. Composition as claimed in claim 6, wherein the composition contains p16 and p26 proteins of said virus.
- 42. Composition as claimed in claim 41, wherein the composition contains pl6 and  $\bf p26$  proteins and  $\bf gp130-140$  glycoproteins of said virus.
- 43. Composition as claimed in claim 6, wherein the composition contains gp36 glycoprotein of said virus.
- 44. Composition as claimed in claim 6, wherein said composition contains 10 to 500 micrograms of said protein and glycoprotein.
- 45. Composition as claimed in claim 6, wherein said composition contains 10 to 50 micrograms of said protein and glycoprotein.
- 46. Composition as claimed in claim 6, wherein said composition contains a pharmaceutically acceptable vehicle.
- 47. Isolate of a retrovirus, wherein the retrovirus has the identifying characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-502.
- 48. Isolate of a retrovirus, wherein the retrovirus has the identifying characteristics of the virus deposited under culture collection accession number C.N.C.M. No. I-532.

L52 ANSWER 41 OF 41 USPATFULL on STN

89:1219 Method of inhibiting  ${f HIV}$ .

Lifson, Jeffrey D., Menlo Park, CA, United States McGrath, Michael S., Burlingame, CA, United States Yeung, Hin-Wing, Kowloon, Hong Kong Hwang, Kou M., Danville, CA, United States

Gene Labs, Inc., Redwood City, CA, United States (U.S. corporation)Regents of University of California, Berkeley, CA, United States (U.S. corporation) US 4795739 19890103

APPLICATION: US 1987-56558 19870529 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- 1. A method of inhibiting expression of  ${\bf HIV}$  antigens in human T lymphocytes and monocyte/macrophage cells infected with  ${\bf HIV},$  comprising exposing the infected cells to an anti- ${\bf HIV}$  protein selected from the group consisting of trichosanthin or momorcharin, at a protein concentration which is effective to produce a substantial reduction in viral  ${\bf antigen}$  expression in  ${\bf HIV}\text{-infected}$  cells.
- 2. The method of claim 1, whrein the concentration of the anti-HIV protein is between about 0.05 to 10  $\mu$ g/ml, and is effective in vitro in selectively reducing the number of viable HIV-infected cells, relative to noninfected cells of the same type.
- 3. The method of claim 1, for use in inhibiting **HIV** replication in the infected cells, as evidenced by a reduction, several days after exposure to the anti-**HIV** protein, in reverse transcriptase associated with the infected cells.
- 4. The method of claim 1, wherein one of the **HIV** antigens which is inhibited is **HIV** envelope protein gpl20, as evidenced by reduced binding to infected T cells of an anti-**HIV** antibody present in the serum of an **HIV**-seropositive individual.
- 5. The method of claim 1, wherein one of the **HIV** antigens which is inhibited is **HIV** core protein **p24**, as evidenced by reduced binding of anti-**p24** antibodies to permeabilized **HIV**-infected monocyte/macrophages.
- 6. A method of treating a human subject infected with **HIV**, comprising administering to the subject a dose of an anti-**HIV** protein selected

concentration of anti-HIV protein sufficient to produce a substantial reduction in viral antigen expression in the patient's HIV-infected cells.

- 7. The method of claim 6, wherein the anti-HIV protein is administered in parenteral form.
- 8. The method ff claim 7, wherein the amount of anti-HIV protein administered, as a single dose, is between about 1.5 to 15 mg.
- 9. The method of claim 7, wherein the drug is administered repeatedly, at suitable intervals, until a desired reduction in viral **antigen** expression is achieved.
- 10. The method of claim 7, wherein the reduction in viral **antigen** is evidenced by reduced binding to the subject's infected T cells of an anti-HIV **antibody** present in the serum of an **HIV**-seropositive individual.
- 11. The method of claim 7, wherein the reduction in viral **antigen** is evidenced by reduced binding of anti-**p24** antibodies to permeabilized **HIV**-infected monocyte/macrophages derived from the subject.
- 12. The method of claim 6, which further includes repeating said administering at suitable intervals, assaying the subject for the presence of **antibody** against the administered protein, and administering a second anti-HIV protein selected from the same group if **antibody** against the first-administered protein is detected.
- 13. The method of claim 6, wherein the concentration of anti-HIV protein is sufficient to effect a selective reduction in the number of HIV-infected cells, relative to uninfected cells of the same type.

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L27

26 S E3

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L5
             10 S L4 AND ANTIBOD?
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L52
=> log off
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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF LOGOFF? (Y)/N/HOLD:y

STN INTERNATIONAL LOGOFF AT 08:18:25 ON 24 JUL 2006

12/06/00 - 020

USSN: Divisional of 09/731,126 Attorney Docket No.: 6755.US.D1 Preliminary Amendment Page 3

ilintos

# Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

CLHS 27-39

Claims 1-26 (canceled)

Claim 27 (currently amended): A method of detecting 1) one or more antibodies selected from the group consisting of <u>Human Immunodeficiency Virus-1</u> (HIV-1) antibody and <u>Human Immunodeficiency Virus-2</u> (HIV-2) antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of:

a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes;

P24 Abs CAPTURE

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- b) detecting said HIV-1 antigen/HIV-1 antibody complexes, presence of said complexes indicating presence of HIV-1 antibody in said test sample;
- c) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes;
- d) detecting said HIV-2 antigen/HIV-2 antibody complexes, presence of said complexes indicating presence of HIV-2 antibody in said test sample;

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- e) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; and
- f) detecting said complexes, presence of said complexes indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in said test sample.

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Claim 28 (original): A method of detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing said one or more of said antibodies and one or more of said antigens, comprising the steps of:

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- a) contacting said test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes:
- b) adding a conjugate to the resulting HIV-1 antigen/HIV-1 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal;
- c) detecting HIV-1 antibody which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of HIV-1 antibody in said test sample;

HEW-2 AS CAPTURE .

- d) contacting said test sample with at least one HIV-2 antigen which binds to HIV-2 antibody for a time and under conditions sufficient for the formation of HIV-2 antigen/HIV-2 antibody complexes:
- e) adding a conjugate to the resulting HIV-2 antigen/HIV-2 antibody complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody, wherein said conjugate comprises an antigen attached to a signal generating compound capable of generating a detectable signal;
- f) detecting HIV-2 antibody which may be present in said test sample by detecting a signal generated by said signal-generating compound, presence of said signal indicating presence of HIV-2 antibody in said test sample;

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HID-1/2 Ay CAPTURE ASSAY g) contacting said test sample with at least one monoclonal antibody which binds to a shared epitope of Human Immunodeficiency Virus-1 protein 24 and Human Immunodeficiency Virus-2 protein p26 for a time and under conditions sufficient for the formation of antibody/antigen complexes; h) adding a conjugate to the resulting antibody/antigen complexes for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen, wherein said conjugate comprises an antibody attached to a signal generating compound capable of generating a detectable signal; and i) detecting presence of antigen which may be present in said test sample by detecting a signal generated by said signal generating compound, presence of said signal indicating presence of at least one antigen selected from the group consisting of HIV-1 antigen and HIV-2 antigen in said test sample.

Claim 29 (new): The method of claim 27 wherein said at least one HIV-1 antigen of step a) is a core antigen.

Claim 30 (new): The method of claim 29 wherein said core antigen is p24.

Claim 31 (new): The method of claim 27 wherein said at least one HIV-2 antigen of step c) is a core antigen. 660?

Claim 32 (new): the method of claim 31 wherein said core antigen is p26.

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Claim 33 (new): The method of claim 27 wherein said at least one monoclonal antibody of step e) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.

Claim 34 (new): The method of claim 28 wherein said at least one HIV-1 antigen of step a) is a core antigen.

Claim 35 (new): The method of claim 34 wherein said core antigen is p24.

Claim 36 (new): The method of claim 35 wherein said at least one HIV-2 antigen of step d) is a core antigen.

Claim 37 (new): The method of claim 36 wherein said core antigen is p26.

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Claim 38 (new): The method of claim 28 wherein said at least one monoclonal antibody of step g) is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.

Claim 39 (new): The method of claim 28 wherein said antibody of step g) of said conjugate is selected from the group consisting of 120A-270, 115B-151, 117-289, 103-350, 115B-303 and 108-394.

## Amendments to the Specification:

Please amend the specification as follows:

On page 1, line 3, please add the following paragraph under the title:

The present application is a divisional of pending U.S. patent application Serial No. 09/731,126, filed December 6, 2000, hereby incorporated in its entirety by reference.

Please replace the paragraph on page 17, lines 17-32 with the following paragraph:

The present invention not only includes the monoclonal antibodies referred to above but also includes the novel hybridomas cell lines which produce these antibodies. More specifically, the cell line ATCC HB \_\_\_\_ PTA-3980 (deposited with the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110 under the terms of the Budapest Treaty on December 4, 2001) produces monoclonal antibody 120A-270, the cell line ATCC HB \_\_\_\_ PTA-2809 produces monoclonal antibody 115B-151, the cell line ATCC HB \_\_\_\_ PTA-2806 produces monoclonal antibody 117-289, the cell line ATCC HB \_\_\_\_ PTA-2808 produces monoclonal antibody 103-350, the cell line ATCC HB \_\_\_\_ PTA-2807 produces monoclonal antibody 108-394, and the cell line ATCC HB \_\_\_\_ PTA-2810 produces monoclonal antibody 115B-303. The cell lines producing the last five antibodies noted were deposited with the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110 under the terms of the Budapest Treaty on \_\_\_\_\_ December 13, 2000 and were accorded the ATCC accession numbers noted above.

but non identical HIV core proteins. Simple cross reactivity of monoclonal antibodies is likely to be insufficient to achieve equivalent quantitative detection of HIV core proteins. Rather, shared reactivity in combination with high affinity is required to achieve the desired result. The affinity of a monoclonal for a related core protein may be substantially lower than that determined with the immunizing core protein. In that case, the epitope is most likely cross-reactive and the 10 affinity of the antibody for the cross-reactive epitope may severely limit the utility of the antibody for detection of diagnostically relevant (i.e., 25pg p24/ml serum or plasma, Courouc·, et al., La Gazette de la Transfusion (1999) N° 155-Mars-Avril) concentrations of the cross reactive core protein. 15

There are currently no known descriptions of

immunoassays using only 2 monoclonal antibodies to achieve equivalent quantitative detection of HIV-1 Group M, HIV-1 Group O, and HIV-2 core proteins. Thus, such an 20 immunoassay is certainly desirable. Two or more monoclonals in combination with polyclonal sera (immunoglobulin) have provided the basis for immunoassays to detect HIV-1 core protein or simultaneously HIV-1 and HIV-2 core proteins (Mehta, et al., U.S. Patent No. 5,173,399; Butman, et al., U.S. Patent No. 5,210,181; Butman, et al., U.S. Patent No. 5,514,541; Kortright, et al., U.S. Patent Nol 4,888,290; Kortright, et al., U.S. Patent No. 4,886,742; Gallarda, et al. W093/21346). Thus, in view of the above, previous literature fails to (a) describe or teach immunoassay restricted to two monoclonals for equivalent quantitative detection of HIV-1 Group M and HIV-2 core proteins, (b) describe or teach immunoassays restricted to two monoclonal antibodies for equivalent quantitative detections of HIV-1 group M, HIV- from the group consisting of HIV-1 antigen and HIV-2 antigen in a test sample comprising: (a) at least one monoclonal antibody which which specifically binds to Human Immunodeficiency Virus-1 protein p24 and Human Immunodeficiency Virus-2 protein p26; and (b) a conjugate comprising an antibody attached to a signal-generating compound capable of generating a detectable signal. The at least one monoclonal antibody of (a) may be, for example, 120A-270, 115B-151, 117-289, 108-394, 115B-303, or 103-350, and is preferably 120A-270. The antibody of (b) may be, for example, 120A-270, 115B-151, 117-289, 108-394, 115B-303, or 103-350, and is preferably 115B-151.

The present invention also includes a diagnostic reagent comprising at least one monoclonal antibody selected from the group consisting of 120 A-270, 115B-151, 117-289, 103-350, 108-394 and 115B-303.

Additionally, the present invention encompasses isolated epitopes or peptides having the amino acid sequences shown in SEQ ID Nos: 1-6.

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The present invention also includes methods of simultaneously detecting both antigen and antibody to HIV-1 and/or HIV-2 in a patient sample. One such method involves detecting 1) one or more antibodies selected from the group consisting of HIV-1 antibody and HIV-2 antibody, and 2) one or more antigens selected from the group consisting of HIV-1 antigen and HIV-2 antigen, in a test sample suspected of containing one or more of the antibodies and one or more of said antigens, comprising the steps of: a) contacting the test sample with at least one HIV-1 antigen which binds to HIV-1 antibody for a time and under conditions sufficient for the formation of HIV-1 antigen/HIV-1 antibody complexes; b) detecting the HIV-1 antigen/HIV-1 antibody complexes, presence of the